

# ABSTRACTS OF WORLD MEDICINE

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## Hygiene and Public Health

### 1. The Care of the Chronic Sick. V. (Investigation of 393 Patients Seeking Admission to a Hospital for the Chronic Sick)

C. R. LOWE. *British Medical Journal* [Brit. med. J.] 2, 699-702, Sept. 23, 1950. 2 refs.

An analysis of the social and domestic circumstances of the in-patients in the largest hospital for the chronic sick in the Birmingham region showed that if the need for frequent medical attention and for skilled nursing were regarded as the criterion of suitability for hospital admission, three-fifths of the patients could have been cared for outside hospital, had certain essential complementary facilities been available. Findings about patients already in hospital, however, could not be accepted as a guide to future policy or to the relative responsibility of different bodies for the care of the chronic sick in the light of recent legislation. An analysis was therefore made of the domestic circumstances and medical condition of 335 patients for whom admission to the hospital was sought between October 10 and December 22, 1949, inquiries being made by an almoner in the home within 24 hours of application, and the medical examination being carried out at home or shortly after admission to hospital.

Four categories were distinguished. Into the first group, which constituted 40% of the total, fell those patients who needed skilled nursing or medical attention, or both, not less frequently than once a week. They were either acutely ill, needed hospital investigation, or were in the terminal stages of malignant disease. The second group (10%) was mostly made up of senile demented patients, who needed admission to a mental institution as, because of their abnormal mental state, they needed personal supervision. More than half of them were old people who were both bed-fast and incontinent. The third group (24%) consisted of persons not requiring skilled nursing or weekly medical attention, but who could not be kept in their own homes. One-third of them had no pathological lesion and suffered merely from infirmity associated with advanced age. Nearly all the rest were partially incapacitated by illness; they did not need the special services available in the hospitals, but, on the other hand, they required more attention than could be provided at home or in municipal homes for the aged. Such patients would be suitable for accommodation in "long-stay annexes" associated with general or special hospitals. The social circumstances of those in the fourth group (26%) were such as to permit of their being cared for at home. This group required little medical attention and, although a few

needed visiting more than once a week, most could be supervised by fortnightly or less frequent visits. Only about 16% of the group required skilled nursing (insulin injections, dressings, etc.), while nearly one-half needed no nursing at all. To enable such patients to be looked after at home, however, it is necessary to have not only an efficient home-nursing and home-help service, but also adequate housing, including a bath and hot water. The rising demand for hospital accommodation can be stemmed only if there is a marked improvement in national housing standards.

Caryl Thomas

### 2. The Persistence of Dust in Occupied Rooms

E. J. LOWBURY. *Journal of Hygiene* [J. Hyg., Camb.] 48, 1-5, March, 1950. 1 fig., 8 refs.

As a preliminary study of the survival of bacteria in floor dust, experiments were designed to investigate the persistence of dust in rooms. Small amounts of insoluble fluorescein, as a powder or precipitated in blanket wool, were scattered in rooms which were thoroughly dusted daily. Measurable quantities were detectable in the floor sweepings for 3 weeks.

Scott Thomson

### 3. The Survival of Bacteria in Dust. I. The Distribution of Bacteria in Floor Dust. II. The Effect of Atmospheric Humidity on the Survival of Bacteria in Dust. III. The Effect of Light on the Survival of Bacteria in Dust. IV. Atmospheric Humidity and the Bactericidal Action of Ultra-violet Irradiation

O. M. LIDWELL and E. J. LOWBURY. *Journal of Hygiene* [J. Hyg., Camb.] 48, 6-43, March, 1950. 7 figs., bibliography.

(1) Floor dust was collected from the wards of isolation hospitals, houses, and schoolrooms, and the fine dust was separated from the fluff by a sieve, as the former was found to harbour more bacteria. Weighed portions were examined by replicate tests after shaking in fluid with glass beads. The distribution of counts suggested that bacteria were present in aggregates, which were broken down by shaking in this way; more elaborate methods did not appear to break down the aggregates any more efficiently. The distribution of counts in replicate tests approximated to a log-normal form and this relation held for pathogens (*Streptococcus pyogenes* and *Staphylococcus aureus*) as well as for non-pathogens.

(2) Floor dust containing *Staphylococcus aureus* and *Streptococcus pyogenes* was exposed for long periods to atmospheres of different humidities. The fall in bacterial population showed a positive correlation with humidity

(a possible exception has been found in the case of *Bacterium coli*). The death rate increased more rapidly with relative humidity at high humidities, but there was no maximum death rate at any particular relative humidity.

Bacteria in dust survived longer in a cupboard than in a refrigerator where the relative humidity was between 75 and 90%, the disadvantage of high humidity outweighing the advantage of low temperature.

(3) Although the lethal effect of ultraviolet light on bacteria is much reduced if the bacteria are fixed to dust, it does not follow that such exposure is without effect. Bacteria-laden dust was exposed to ultraviolet light, fluorescent lighting, tungsten lighting, and daylight for long periods. Tungsten light was without effect, but the activity of the others was definite though limited, being greater in the first 10 days than thereafter.

(4) In very dry atmosphere the effect of all the radiations was reduced. At ordinary humidities in rooms, low-intensity ultraviolet light or fluorescent lighting of good intensity destroyed various organisms at a rate five times that experienced in the dark.

The bactericidal effect of ultraviolet light on dried films of *Streptococcus pyogenes* varied with relative humidity and the medium in which the streptococci had been suspended before drying. The death rate was initially logarithmic, but frequently slowed down and surviving organisms seemed to possess a degree of resistance. The death rates of *Strep. pyogenes* in these preparations were greater than those found in floor dust.

Scott Thomson

#### 4. Static Pressure and Ventilation Rates in Rooms

F. W. BLACK. *Journal of Hygiene [J. Hyg., Camb.]* 48, 44-51, March, 1950. 6 figs., 7 refs.

#### 5. The Dermatophytoses of Great Britain. Report of a Three Years' Survey

J. WALKER. *British Journal of Dermatology and Syphilis [Brit. J. Derm. Syph.]* 62, 239-251, June, 1950. 1 fig., 20 refs.

A survey on as comprehensive a scale as possible of the present state of ringworm infections in Great Britain is described in detail. The types obtained from the various lesions, the numbers of each dermatophyte cultured, the age and sex incidence, and the probable sources of infection were investigated. The observations bear out the historical record of a great preponderance of the small-spore type of infection in England. In addition to an increase in indigenous infections, the return of large numbers of people from war-time service abroad has resulted in the introduction of new infections which themselves tend to become established and indigenous.

The author comes to the conclusion that the unavoidable relaxation of control and treatment of tinea capitis during the war has brought about a reversion to the conditions existing at the beginning of the century before the introduction of x rays. The geographical distribution of the different species of *Microsporum* is illustrated on a map.

G. B. Mitchell-Heggs

#### 6. Survival of Tubercle Bacilli in Various Sewage Treatment Processes. I. Development of a Method for the Quantitative Recovery of Mycobacteria from Sewage

D. PRAMER, H. HEUKELEKIAN, and R. A. RAGOTZKIE. *Public Health Reports, Washington [Publ. Hlth Rep. Wash.]* 65, 851-859, July 7, 1950. 15 refs.

The authors have devised a method for the quantitative estimation of tubercle bacilli in sewage; by their technique about 90% of the sewage organisms normally present can be suppressed. This method, which is described in detail, was employed to assess, in a laboratory experiment, the effect of various sewage treatments on the survival of tubercle bacilli. Chemical coagulation with ferric chloride and continuous sand filtration were highly effective. Chlorination was satisfactory only when a concentration of at least 0.9 part of free chlorine per million was attained. In a preliminary field trial, sanatorium sewage which was processed by sedimentation, trickling filtration, and chlorination was examined at various stages. Acid-fast bacilli were found in the plant effluent and the stream receiving it, as well as in the raw and digested sludge.

W. G. Harding

#### 7. Lung Carcinoma in Iceland

N. DUNGAL. *Lancet [Lancet]* 2, 245-247, Aug. 12, 1950. 13 refs.

Lung cancer is relatively rare in Iceland and was found in only 12 out of 337 necropsies on cases of carcinoma performed in Reykjavik during the period 1932-48. These 12 cases were distributed more or less evenly over the period concerned, affording no evidence that the disease is increasing in frequency in Iceland. If it be assumed that cigarette smoking is an important cause of lung cancer, this may explain the continued rarity of the disease in Iceland, where until recent years the consumption of cigarettes was relatively small.

R. A. Willis

#### 8. Cancer of the Stomach in the Large Towns of England and Wales, 1921-39

P. STOCKS. *British Journal of Cancer [Brit. J. Cancer]* 4, 147-157, June, 1950. 3 refs.

A statistical analysis is made of the deaths from cancer of the stomach in the 83 county boroughs of England and Wales during the years 1921-39. The stomach-cancer death rates in these towns show very large differences, considerably more than could be expected to occur by chance. These differences are apparent at all ages; in fact the differences are greatest at ages between 25 and 55 in males and at ages up to 65 in females. These relations with age are just the reverse of what would be expected if the differences in mortality arose merely from differing accuracy of death certification, which should exert its maximum effect in old age. It is also found that the recorded death rates from stomach cancer show no association with the death rates in the same towns from other digestive diseases—rates which would include wrongly certified cancer deaths. The differences appear, therefore, to be real. The high rates of mortality tend to appear in the northern towns rather than the southern and are positively correlated with the



proportion of unskilled workers in the population. Grouping the towns according to the hardness of their water supply reveals rather higher rates in those with very soft or very hard water, and lower rates intermediately. The facts appear to be consistent with the hypothesis that the development of gastric cancer depends on an irritant whose latent period is shorter in some towns than in others.

A. Bradford Hill

9. **A Q Fever Epidemic in the Swiss Railway Works, Zürich-Altstetten. Observations on the Epidemiology and Symptomatology of Q Fever.** (Über eine Q-Fieber-Epidemie in der SBB-Werkstätte Zürich-Altstetten. Beitrag zur Epidemiologie und Symptomatologie des Q-Fiebers)

G. BRACHER. *Praxis [Praxis]* 39, 253-254, March 23, 1950.

Fourteen serologically-positive cases of Q fever occurred in the winter of 1948-9 among employees of the railway works in Zürich. All the patients worked in a building in which the air was contaminated by dust from the car-cleaning department of the neighbouring slaughterhouse. Complement-fixation reactions for Q fever were also positive in 19 of the 110 employees of the slaughterhouse and in 3 out of 57 employees of the department in which hides and fat were processed. The incidence of positive reactions was higher among persons having contact with live cattle. Positive serological reactions were also found in 7 out of 10 cases of influenza among railway employees engaged in unloading cattle.

O. Gsell (*Excerpta Medica*)

## INDUSTRIAL MEDICINE

10. **The Effect of Wood Dust on the Lungs.** (Inverkan av trädamms på lungorna)

Å. VALLANDER. *Nordisk Medicin [Nord. Med.]* 44, 1315-1317, Aug. 18, 1950. 1 fig., 10 refs.

The author has examined the workers employed for 10 years or more in the Varnamo timber industry (81 in all). Apart from radiological evidence of calcified primary foci and old pleurisy (6 cases) only 2 men were found to have abnormal signs in the chest: one had asthma, the other chronic bronchitis with emphysema and pulmonary fibrosis. The author considers that exposure to sawdust is unlikely to have been an aetiological factor in either of these cases and that there is no risk of pneumoconiotic changes associated with such employment.

W. G. Harding

11. **Histological Studies of the Effects of Beryllium Oxide (Glucine) on Animal Tissues**

A. POLICARD. *British Journal of Industrial Medicine [Brit. J. industr. Med.]* 7, 117-121, July, 1950. 7 figs., 8 refs.

Beryllium oxide dust from a hydroelectric plant in Savoy was introduced into the lungs of rats and guinea-pigs by rotation dusting and by intratracheal injection. Subcutaneous and intraperitoneal injections of suspensions of the dust were also made and the tissues subsequently examined microscopically. The dusts

were of less than 1- $\mu$  particle size; one specimen was pure and one was contaminated with fluoride. A simple method of histochemical differentiation by means of van Gieson stain and polarized light is described. Histologically, the dust particles were always conglomerated. The fluoride-contaminated dust provoked necrosis of cells, and often caused a lethal aseptic peritonitis or chemical oedema of the lung. The main tissue reaction to either kind of dust was histiocytic, and a granulomatous nodule was formed, most typically in lung parenchyma. The histiocytes might be very large. In 3 to 6 weeks the granulomata had disappeared, but even 10 months later beryllium oxide could be detected at a site of injection; ultimately it was absorbed, probably by the histiocytes, and eliminated.

J. N. Agate

12. **Chronic Pulmonary Granulomatosis in Residents of a Community near a Beryllium Plant: Three Autopsied Cases**

I. C. CHESNER. *Annals of Internal Medicine [Ann. intern. Med.]* 32, 1028-1048, June, 1950. 7 figs., 15 refs.

Chronic pulmonary granulomatosis, or "delayed chemical pneumonitis", is a form of pneumoconiosis due to beryllium intoxication and is liable to occur not only among workers with beryllium and its alloys, but also in persons living near the factories and among the families of employed persons. Three such cases, all fatal, are described by the author. The lesion is a form of widespread fibrosis of the lungs with nodules, giving a fuzzy radiological appearance. The symptoms resemble those of silicosis and include breathlessness, wasting, and great mental and physical depression. Frequently there is delay between exposure to the metal and the onset of symptoms. Little is known about susceptibility to the disease and the capricious nature of its occurrence cannot be explained. Once present it tends to run a slowly progressive but fatal course, and the possibility of this disease in workers engaged in beryllium production and in industries where beryllium is used, as in the manufacture of radiotherapeutic plant and fluorescent lighting installations, should be kept in mind.

G. F. Walker

13. **Pneumonokoniosis in Queensland Foundries**

D. GORDON. *Medical Journal of Australia [Med. J. Aust.]* 2, 217-224, Aug. 5, 1950. 3 figs., 38 refs.

In 1947 and 1948 seventy-six Queensland foundries, employing 1,100 men, were studied from the point of view of pneumoconiosis. They included iron and non-ferrous foundries and one steel foundry. Moulders who had worked more than 14 years and fettlers who had worked more than 4 years were considered suitable for examination. Out of 388 such men, 359 agreed to co-operate; 203 moulders, 67 fettlers, 42 moulder's assistants, and 47 other foundry workers were examined. Thirteen of these workers were considered to have silicosis, largely on radiological grounds, and in addition 8 cases were considered doubtful. Of the 13 men, 4 were fettlers (2 steel), 4 were furnacemen (2 steel), 3 were moulders, one had a mixed occupational history, and one had been exposed to silica in the coal mines. The author suggests that these results confirm the well-

known fact that in steel foundries the risk is much greater than in other foundries.

The great majority of cases were in elderly subjects. The men were fitters or furnacemen and came from large foundries. Environment studies were carried out on the atmospheric dust; figures are given for dust counts from furnace chipping, the count ranging from 239 to 368 particles of dangerous size (of which 45% was free silica) per c.cm. of air. In the steel foundries highly siliceous parting powders were used.

The author contends that it is incorrect to regard a man with early silicosis as an invalid. *K. M. A. Perry*

**14. Estimation by Spirometry during Effort of Capacity for Work in Silicosis.** (L'estimation de la capacité de travail dans la silicose à l'aide d'enregistrements spirométriques durant l'effort)

E. JÉQUIER-DOGE and M. LOB. *Archives des Maladies Professionnelles* [Arch. Mal. prof.] **11**, 349-356, 1950. 5 figs., 24 refs.

Three persons suffering from silicosis, and in whom the disease was diagnosed in its early stages, underwent tests with the spirometer in order to determine the degree of disability. Tests were made while they were at rest and also when working, the energy output being measured by an ergometer. It was evident that the methods used did not permit close correlation of function with the pulmonary lesions, since circulatory efficiency and the efficiency of tissue respiration were also involved.

In the 3 cases the degree of disability had been estimated clinically, the findings being confirmed by the courts. This fact, and the apparent effect of nervous factors or of unwillingness to co-operate fully, tended to vitiate the experiments. In general, the readings made during physical exertion were more reliable than those obtained during rest. As the experiments were continued for some years, it was noted that results became more reliable, this being largely due to psychic factors but also to improvement as regards superadded symptoms of respiratory catarrh, bronchitis, or bronchial spasm. The harm done by litigation in these cases was reflected at intervals by peculiar variations in the readings.

*G. C. Pether*

**15. A Study of the Excitability of Respiratory and Sympathetic Pulmonary-vascular Centres in Silicosis.** (Étude de l'excitabilité des centres respiratoires et des centres sympathiques vaso-pulmonaires chez les silicotiques)

D. SANTENOISE, J. MATTEI, A. PERRET, and M. ROCHE. *Archives des Maladies Professionnelles* [Arch. Mal. prof.] **11**, 277-283, 1950. 6 refs.

The excitability of the respiratory centre was judged by requiring subjects to breathe air containing increasing proportions of carbon dioxide; respiratory movements were measured mechanically and the concentration of CO<sub>2</sub> was noted at which a considerable increase in amplitude of respiration occurred (an earlier and slighter increase in some subjects was discounted as probably resulting from direct irritation of pulmonary sensory

nerve endings). In normal subjects the depth of respiration increased when the CO<sub>2</sub> content of the inspired air was 2 to 4%. Of 55 untreated miners with silicosis, 54 showed no response to 4% CO<sub>2</sub>, while 8 required over 8% for increase in respiration. A similar group of miners who had been treated in hospital for several months showed reactions at levels closer to the normal.

Compression of the abdomen led to rise in systemic diastolic pressure and diminution in systolic pressure in 108 out of 127 silicotic miners who had received no treatment. This type of reaction is interpreted by the authors as evidence of hyperexcitability of sympathetic vasoconstrictor nerves in the pulmonary circulation. A similar type of reaction was observed in 21 of 36 miners who appeared to have early silicosis but were still able to work.

The authors suggest that these modifications of nervous excitability may precede the radiological appearance of silicosis, and may afford the earliest means of diagnosis. On the other hand, it is possible that subjects who possess an abnormal excitability may be more prone to develop silicosis.

*H. E. Harding*

**16. Hazards in the Use of Radioactive Static Eliminators and their Control**

J. E. SILSON. *American Journal of Public Health* [Amer. J. publ. Hlth] **40**, 943-952, Aug., 1950. 9 figs., 5 refs.

Static electricity is created in the course of many industrial processes, particularly where paper, plastics, and rubber are handled; this may create dangerous risks in industry. For example, in the rubber-coating of fabrics a heavy static discharge develops on the sheet being coated as it passes between spreading rollers. The solvents used in the rubber-coating industry are very inflammable, and a spark might cause a serious fire or an explosion.

Recently, bars of radioactive substances have been used to ionize the air, the substances being either polonium or radium. Radium bars have a half-life of about 1,600 years, so that once installed they require no further replacement. Beta radiation is easily controlled by shielding, which can be accomplished by a properly designed housing for the radium bar. Protection against gamma radiation involves the maintenance at all times of a minimum distance between the worker and the source, since shielding is generally impracticable because of the great thickness of lead required. In general, safe working exposure can be obtained by the maintenance of an 18-in. (45-cm.) distance between the worker and the heaviest bar used.

Polonium has a short half-life and produces a hazardous radioactive dust; this is therefore not so useful. Workers employed in industries where radioactive static eliminators are used should therefore be under constant medical supervision; film-badge monitoring is the only reliable check on the actual dose which they are receiving.

*K. M. A. Perry*

**17. Studies in Occupational Morbidity: Part III**

I. SUTHERLAND, C. G. HARRIS, and A. SMITHERS. *British Journal of Industrial Medicine* [Brit. J. industr. Med.] **7**, 140-144, July, 1950. 1 fig., 2 refs.

# Physiology and Biochemistry

## 18. Total Body Water in Man

J. M. STEELE, E. Y. BERGER, M. F. DUNNING, and B. B. BRODIE. *American Journal of Physiology* [Amer. J. Physiol.] **162**, 313-317, Aug., 1950. 14 refs.

Total body water was measured by determination of the volume of dilution of "antipyrine" (phenazone) in a group of 51 normal men (ages 24 to 96 years) and 31 women (ages 21 to 94 years). In the men the average value was 53% of the body weight (range 40 to 68%) and in the women 45% (range 30 to 53%), and the variations between individuals are considered to be correlated with variations in degree of obesity. There was no correlation between age and total body water. Determinations in a group of oedematous individuals showed a range of 58 to 71% of body weight, 5 values lying within the range for normal males.

F. W. Chattaway

## 19. Estimation of Intracellular Water in Man

E. Y. BERGER, M. F. DUNNING, J. M. STEELE, R. JACKENTHAL, and B. B. BRODIE. *American Journal of Physiology* [Amer. J. Physiol.] **162**, 318-325, Aug., 1950. 1 fig., 17 refs.

Values for the volume of intracellular water obtained by determining the difference between total body water, as indicated by the degree of dilution of "antipyrine" (phenazone), and extracellular water, as represented by the volume of distribution of bromide, are clearly too small. Inulin space was measured in dogs after nephrectomy and in human subjects with severe renal insufficiency by allowing 20 hours for equilibration after administration of the inulin, and in patients with normal renal function by establishing equilibrium by continuous infusion of inulin and then determining the amount of inulin excreted after the time of stopping the infusion, a correction being applied to allow for inulin retained in the ureters, kidney pelves, and tubules at that moment. Bromide space was determined in the same subjects.

Values for bromide space were considerably higher than for inulin space, and the former is not considered to represent only extracellular water; this last was found, on the basis of inulin determinations, to be 15% of body weight in 4 subjects, intracellular water being 40% of body weight.

F. W. Chattaway

## 20. Observations on Drinking Induced by Hypertonic Solutions

J. H. HOLMES and M. I. GREGERSEN. *American Journal of Physiology* [Amer. J. Physiol.] **162**, 326-337, Aug., 1950. 1 fig., 15 refs.

Thirst was induced in a group of 40 adult mongrel dogs by injection of hypertonic solutions of a number of substances, and water consumption and urine excretion were determined over the following 4 hours, together with any changes in haematocrit value and levels of

protein, sodium, and chloride in plasma. Of the 40 dogs 16 had closed cannulae leading to the stomach. When solutions of 5, 10, 15 or 20% sodium chloride (2.5 ml. per kg. body weight) were used, considerable variation in the amount of water consumed was found, but results of a number of experiments with the same dog were consistent; injection of 0.9% sodium chloride produced no water consumption. The volume of water consumed bore no relation to the amount required to dilute the injected salt solution to isotonicity, and the water was taken by some dogs within 5 minutes of the injection, by others in small amounts spread over  $\frac{1}{2}$  to 1 hour; by 2 dogs no water was consumed for 10 minutes. Injection of pitressin (10 pressor units), 15 to 20 minutes before the injection of salt delayed the onset of drinking. Introduction of water into the stomach 20 to 30 minutes before injection of the hypertonic solution prevented any drinking after injection, but with administration at the time of injection the animal drank as usual. If the water ingested after a salt injection is withdrawn at once, drinking is resumed in 3 to 5 minutes. Vagotomy and spinal-cord section at the levels of the first or second thoracic segment did not modify the responses. Sorbitol, sucrose, and isomolar solutions of sodium sulphate and acetate produced results similar to those with sodium chloride, but glucose was much less effective.

F. W. Chattaway

## 21. Role of Sodium and Chloride in Thirst

J. H. HOLMES and M. I. GREGERSEN. *American Journal of Physiology* [Amer. J. Physiol.] **162**, 338-347, Aug., 1950. 3 figs., 15 refs.

Four dogs with gastric fistulae were used to study the role of sodium and chloride in thirst induced by injection of 20% sodium chloride solution. Thirst does not depend on the level of these ions in the blood, for (a) the amount of water consumed varied in different dogs, although the rise in serum level of sodium and chloride was the same, (b) the amount consumed is the same whether drinking was permitted at once or after 4 hours, and (c) drinking was often completed in 5 minutes, too soon for any changes in blood electrolyte level to have occurred.

F. W. Chattaway

## 22. Circulation Time in Various Sections of the Circulatory System. (Скорость кровотока в отдельных участках системы кровообращения)

Z. I. MODESTOVA. *Клиническая Медицина* [Klin. Med., Mosk.] **28**, No. 5, 52-59, May, 1950. 6 refs.

The method of measuring the circulation time employed by this investigator was by intravenous injection of fluorescein. With the help of three assistants, drops of blood are collected on strips of filter paper at one-second intervals from three sites; (a) the lobe of an



ear; (b) the tip of a finger; (c) the cubital vein of the opposite elbow to that into which the dye is injected (a sterilized 20% solution is used). The first reading gives the circulation time in the lesser circuit; (b) minus (a) gives that in the arterial tree plus the capillary bed; (c) minus (b) gives that in the venous section. The details of the whole proceeding are described in the article; a metronome, calibrated with a stop-watch, is used for timing the collection of drops. By measuring the number of drops taken before the dye appears, the time in seconds can be calculated after the strips have been examined with a Wood filter and a quartz lamp.

Four groups of subjects were investigated: (1) 21 persons, either healthy or with well-compensated heart lesions; (2) 40 with cardiovascular disease and circulatory failure of first, second, or third degree (Strazhesko's classification); (3) 50 with pneumosclerosis and 7 with pneumonia; (4) 75 with essential hypertension in three stages—compensated, decompensated, or associated with marked dyspnoea.

The circulation times in the healthy controls were: total circulation (arm-to-arm), 24.2 seconds; lesser circuit, 10.5 seconds; arterio-capillary, 6.2 seconds; venous, 7.5 seconds. In the cases of cardiovascular disease, all three sections of the circulation showed retardation of flow (59.3, 23.3, 18.5, and 17.5 seconds respectively in the third stage of failure, with correspondingly less retardation in milder disease). In the cases of pneumosclerosis there was retardation in the arterial and venous sections, but in those with signs of cardiac failure only the pulmonary circuit was affected. In the patients with pneumonia, the venous circulation times were normal. In hypertension, all the circulation times were increased with each successive grade of severity; the venous and pulmonary times each formed a smaller percentage of the total. This the author explains as being due to initial failure of the left ventricle. [It may well be due to delay in the arterioles.]

L. Firman-Edwards

### 23. Venous Velocity of the Leg Measured with Radioactive Sodium

J. E. LEVI and E. F. LEWISON. *Bulletin of the Johns Hopkins Hospital [Bull. Johns Hopk. Hosp.]* 86, 370-382, June, 1950. 4 figs., 27 refs.

At the Mount Sinai Hospital, Baltimore, the authors investigated the linear venous velocity (the rate of venous blood flow along a given segment of vein) in the lower limbs of 40 normal subjects under standard conditions. Credit is given to Payling Wright *et al.* for the first direct studies with radiosodium of venous circulation in the lower limbs, at University College Hospital, London. A small volume (0.1 to 0.2 ml.) of hypertonic sodium chloride solution with specific activity of less than 75 microcuries was injected into the greater saphenous vein at the ankle and its time of arrival at the groin determined with a Geiger-Müller counter and standard counting equipment. The mean velocity for the group was  $3.8 \pm 0.37$  cm. per second, but the values ranged from 1.3 to 13 cm. per second. No age or sex difference was noted. In 18 cases a localized

"puddling" of radioactivity was observed in the calf; in one such case opportunity presented of dissecting the leg and it was noted that at the exact site of "puddling" a tributary vein entered the greater saphenous vein at an unusually obtuse angle.

Attention is drawn to the neglect of the study of mechanical aspects of venous stagnation and to their contribution to the development of thrombosis and embolism. The method used offers an objective method of measurement of the venous circulation. The authors intend to carry out further studies in cases of prolonged rest in bed after operation, and in cases with clinical evidence of venous thrombosis and pulmonary embolism. [The records only of single observations on each patient are recorded. No mention is made of the variation in value on repeated observation on the same limb, and no comparison is made of the values found in the two limbs in the same individual.] Edwan M. McGirr

### 24. Stability of Body Function in the Aged. I. Effect of Exposure of the Body to Cold

C. L. KRAG and W. B. KOUNTZ. *Journal of Gerontology [J. Gerontol.]* 5, 227-235, July, 1950. 2 figs., 14 refs.

Thirteen elderly inmates of St. Louis City Infirmary Hospital, Missouri, were the subjects of this experiment, 6 healthy volunteers, aged 22 to 36, acting as controls. The patients were aged from 57 to 91 years, and though none was bedridden or suffered from acute illness, all were debilitated in some degree.

Under fasting basal conditions they were exposed, unclothed and motionless, to temperatures of 5° to 15° C. (41° to 59° F.) for between 45 and 120 minutes in a modified Burdick fever cabinet. Serial estimations were made of oxygen consumption and body temperature (oral, rectal, and skin surface).

The aged were less able to maintain their body temperature than the young, although the increase in oxygen consumption which occurs in both groups was of earlier onset in the aged. It is inferred that the mechanism of prevention of heat loss [as by contraction of skin vessels] is less efficient in the old than in the young. There was no correlation between the ability to maintain body temperature and the clinical degree of debility.

[It would be unwise to draw general deductions from this experiment conducted on a small group of debilitated hospital patients.] P. D. Bedford

### 25. A Comparative Study of the Metabolic Effects of Pituitary Adrenocorticotrophic Hormone (ACTH) and Cortisone. (Étude comparée des effets métaboliques de l'A.C.T.H. et de la cortisone)

R. S. MACH, P. DUCOMMUN, J. FABRE, R. BORTH, and J. BARAZZONE. *Schweizerische Medizinische Wochenschrift [Schweiz. med. Wschr.]* 80, 692-695, July 8, 1950. 4 figs., 37 refs.

Two cases of rheumatoid arthritis were treated with 100 mg. of cortisone daily for 5 days and, after 2 weeks' interval, with 25 mg. of adrenocorticotrophin (ACTH) daily for 5 days. The pains and ankylosis improved markedly with cortisone—more so than with ACTH.

Urinary output of water, sodium, and chloride was much reduced, weight increased, erythrocyte sedimentation rate and eosinophil count were both lowered, and urinary output of corticosteroids was increased during treatment with both hormones, the effect again being greater with cortisone than with ACTH. Urinary ketosteroid excretion, however, was increased only during administration of ACTH. In 2 other cases, one of polyarthritis and one of familial scleroderma, salt and water balance studies were made, one patient being given four times the above daily dose of ACTH, the other  $2\frac{1}{2}$  times the above dose of cortisone. A positive sodium-chloride and water balance was produced in each case, with an increased output of potassium in the urine and a lowering of the blood potassium level. The effect of ACTH was again to increase the output of ketosteroids [corticosteroid output not stated], whereas cortisone produced an increase in corticosteroid output and a diminution of ketosteroid excretion.

H. K. Goadby

#### 26. The Three Types of "Natural" Diuresis

J. G. G. BORST and L. A. DE VRIES. *Lancet* [*Lancet*] 2, 1-6, July 1, 1950. 6 figs., bibliography.

The excretion of water, sodium, potassium, chloride, creatinine, and urea was studied by the authors in the Department of Medicine, Amsterdam University, in 18 patients who were given an unvarying diet consisting of a measured volume of milk and one or two biscuits with butter every 3 hours. Urine was collected at intervals of exactly 3 hours day and night over periods totalling 500 days.

A rhythmic increase in excretion of water, sodium, chloride, and potassium was observed during the day and a decrease at night. Creatinine and urea excretion were so constant as to suggest that glomerular filtration remained unchanged throughout. The exact timing of the rhythmic fluctuations in output varied slightly according to the time of year. In a patient with Addison's disease the rhythm persisted, but the difference in output between night and day was less marked. Modifications of this basic rhythm were observed in patients with cardiac failure, paroxysmal tachycardia, and cirrhosis of the liver, and could be induced by alterations in posture and other measures, such as blood transfusion, affecting the general circulation.

On the basis of these observations and of other evidence it is suggested that sodium and chloride excretion in particular is sensitive to alterations in the general circulation, an inadequate circulation inducing salt retention, and that the adrenal gland probably plays a major part in this mechanism.

G. M. Bull

#### 27. The Acute Circulatory Effects of the Head-down Position (Negative G) in Normal Man, with a Note on Some Measures Designed to Relieve Cranial Congestion in this Position

R. W. WILKINS, S. E. BRADLEY, and C. K. FRIEDLAND. *Journal of Clinical Investigation* [*J. clin. Invest.*] 29, 940-949, July, 1950. 6 figs., 12 refs.

Circulatory changes were studied in 42 convalescent hospital patients who were subjected to negative accelera-

tions of 1 and 2 "g" on a tilt table. Arterial and venous pressures were determined by direct manometry, cardiac output was calculated from ballistocardiograms, glomerular filtration rate was determined by the inulin or mannitol clearance method, and renal plasma flow by the diodone or *para*-aminohippurate clearance method. The subjective symptoms are described.

When the patient was tilted, an immediate fall in the femoral, and rise in the brachial, arterial pressure was noted; this was assumed to be a passive hydrostatic effect, and was followed by a fall in pressure in both arteries and a slowing and irregularity of the pulse, in which the dicrotic notches became more prominent. The internal jugular venous pressure rose in two stages, a rapid phase being followed by a slow phase; the former was attributed to hydrostatic effects, the latter to drainage of blood from the elevated parts. Venous obstruction of the legs reduced the extent of the second phase. Right auricular pressure recordings followed those of jugular venous pressure, with a difference attributable to the difference in level. Cardiac output and stroke volume increased in the inverted position. No significant change in renal circulation was discovered. Measures to relieve cranial venous congestion in the head-down position are described.

D. H. Sproull

## NUTRITION AND DIGESTION

#### 28. The Clinical Physiology of the Pancreas. (Клинической физиологии поджелудочной железы) N. I. LEPORSKIY. Клиническая Медицина [*Klin. Med., Mosk.*] 28, No. 8, 11-27, Aug., 1950. 10 figs., 5 refs.

In order to study the physiology of the pancreas, the author investigated the amount and composition of gastric and duodenal secretions in healthy subjects and individuals suffering from gastritis, gastric ulcer, and hepatitis. He used a compound tube 1 metre long, consisting of 2 tubes each of 4 mm. diameter, one being 15 to 20 cm. longer than the other and provided with a radio-opaque tip. The secretions were collected at 10-minute intervals with a suction pressure of 35 mm. Hg. The gastric secretions were analysed for amount and acidity, the duodenal for amount and for bilirubin, bicarbonate, and amylase content.

Reflex secretion in the stomach and duodenum was the same in healthy and ill persons; the amounts rose within 30 minutes to about twice the normal and then slowly returned to normal within one hour. Normal subjects showed a higher amount of amylase in the duodenal secretion than did patients with gastric disease.

Giving 2.5 mg. carbachol led to an increase in gastric secretion in all cases; duodenal secretion increased in healthy subjects but not in cases of gastric disease. Amylase content was increased 2 to  $2\frac{1}{2}$  times in all cases. Giving 60 mg. "sympatol" subcutaneously increased gastric secretion in all cases. Duodenal secretion was reduced in healthy subjects and unchanged in cases of gastric ulcer. Amylase content was greatly increased in healthy subjects and only slightly in the others.

Tests were made on 48 people (12 healthy, 13 with

chronic gastritis, 10 with gastric or duodenal ulcer, and 13 with acute hepatitis) during sleep. The tests started at 9 p.m. and finished at 8 a.m. The amount and acidity of gastric secretion were lowered in all cases, in healthy subjects more so than in the others; the smallest fall occurred in cases of duodenal ulcer. Duodenal secretion was lessened in all cases, to the greatest degree in healthy subjects and least in cases of duodenal ulcer. Amylase content rose slightly during the first hours of sleep.

In 25 healthy subjects and 25 persons with acute hepatitis amylase was estimated in the duodenal secretion, blood, and urine. In hepatitis, there was a noticeable decrease (to about 41% of the normal amount) in the amount of duodenal secretion and its amylase content. The decrease occurred gradually during the illness and reached its peak during the third week. Blood and urinary amylase content and gastric secretion did not change in any of the cases. It is thought that an acute or subacute pancreatitis is present in all cases of hepatitis. This is reflected in a decrease of duodenal secretion and its amylase content. *N. Chatelain*

#### 29. The Relationship of Potassium to the Electrolytes and to the Proteins of the Gastric Juice of Man

L. MARTIN. *Gastroenterology* [*Gastroenterology*] 15, 326-340, June, 1950. 4 figs., 29 refs.

At the Johns Hopkins Hospital, Baltimore, a study was made of the potassium content of the resting gastric juice and the juice obtained after the injection of 0.3 mg. of histamine in 35 patients suffering from various digestive and non-digestive disorders. Where stimulation resulted in the secretion of juice containing free acid the concentration of potassium increased, the resting values observed being 11 to 19 mEq. per litre and the highest value after stimulation 35.5 mEq. per litre. The maximum concentration of potassium was observed, on the average, 15 minutes after histamine administration, and the peak of hydrochloric-acid secretion at 30 minutes. The potassium concentration also returned to the resting level before the acid value. The concentration of chloride increased with that of the acid, and the sodium and nitrogen content decreased. In the juice of patients with achlorhydria both before and after histamine stimulation, potassium concentrations of 10 to 27 mEq. per litre were observed, averaging 18.7 mEq. per litre, and there was no significant difference between pre- and post-histamine values. The concentration of sodium was 40.2 to 123.8 mEq. per litre, of chloride 39.0 to 82.6 mEq. per litre and of nitrogen 30 to 139.3 mEq. per litre. Juice obtained by histamine stimulation from 5 patients after vagotomy for duodenal ulcer contained an average of 21 mEq. per litre of potassium when no bile was present, the chloride, sodium, and nitrogen concentrations being similar to those in achlorhydric patients. Of juice obtained from 5 patients by histamine stimulation after partial gastrectomy, the electrolyte pattern in 2 cases was found to correspond with that of juice obtained from intact stomachs. In juice from another patient, in which there was much bile, the electrolyte concentrations in mEq. per litre were: sodium, 98, potassium 3, hydrochloric acid 48, and nitrogen

28. In 2 patients with draining gastric fistulae the serum potassium level was less than 2 mEq. per litre, those of bicarbonate and sodium were raised, and that of chloride was normal. Gastric juice contained 2.3 and 2.4 mEq. of potassium per litre respectively. In hypertensive patients on a low-salt diet no significant changes in the electrolytic pattern of the gastric juice were observed.

The results are considered to indicate that the potassium ion is secreted together with hydrochloric acid in the stomach and that its secretion may represent a function of parietal-gland activity. *R. A. Gregory*

#### 30. Response of Human and Canine Gall Bladder to Cholecystokinin

R. W. DENTON, L. L. GERSHBEIN, and A. C. IVY. *Journal of Applied Physiology* [*J. appl. Physiol.*] 2, 671-679, June, 1950. 1 fig., 8 refs.

Cholecystokinin was prepared from hog duodenal extracts by treatment with trichloroacetic acid and enriched by treatment with aniline. The preparation contained 6 units of cholecystokinin and 6 units of secretin per mg. and was pyrogen-free and non-antigenic. After radiological visualization of the gall-bladder the material was injected intravenously in 8 normal subjects. In 5 subjects evacuation of the gall-bladder occurred when either 66 or 150 cholecystokinin units was given in a single injection. In dogs a reliable dose-response curve could not be obtained, although it seemed that the larger the dose the greater the evacuation. *A. Schweitzer*

#### 31. Effect of Combined Ligation of the Bile Duct and Nephrectomy on Blood Lipids. (Acción combinada de la ligadura del colédoco y la nefrectomía sobre las fracciones lipídicas de la sangre)

C. JIMÉNEZ DÍAZ and H. CASTRO MENDOZA. *Revista Clínica Española* [*Rev. clín. esp.*] 37, 232-235, May 31, 1950. 5 refs.

In 8 dogs combined nephrectomy and ligation of the bile duct resulted in a marked hyperlipaemia, affecting all fat fractions, and an increase in lipid deposition in the liver. Neither of these changes was observed to the same degree after bile-duct ligation alone. The possible significance of these observations is discussed.

[More observations are required to enable the data to be analysed statistically, before the differences described can be regarded as significant. Adequate control experiments do not appear to have been performed.]

*A. C. Frazer*

#### 32. Studies on Amino Acid Excretion in Man. IV Peptic Ulcer

J. B. KIRSNER, A. L. SHEFFNER, W. L. PALMER, and K. STERLING. *Journal of Clinical Investigation* [*J. clin. Invest.*] 29, 867-873, July, 1950. 1 fig., 39 refs.

In 3 normal persons and 4 patients with peptic ulcer the following investigations were carried out at the Frank Billings Clinic, Chicago: nitrogen balance measurements and microbiological assays of leucine, isoleucine, valine, threonine, arginine, histidine, lysine, and methionine in the controlled diet, the plasma, and 6-day collections of urine and faeces. [For technique,



see Sheffner *et al.*, *J. biol. Chem.*, 1948, **176**, 89.] In one control and the 4 patients the plasma proteins were studied electrophoretically.

The only possibly significant finding was an increase in the average concentration of total non-protein amino-acids in the plasma of the 4 patients. This value returned to normal in 2 patients when the ulcer healed. Free amino-acid concentrations were normal. Fast-moving boundaries, apparently abnormal, were found in the electrophoretic patterns of 3 patients. Their significance is not understood.

P. Mestitz

### 33. Studies on Amino Acid Excretion in Man. V. Chronic Ulcerative Colitis and Regional Enteritis

J. B. KIRSNER, A. L. SHEFFNER, and W. L. PALMER. *Journal of Clinical Investigation [J. clin. Invest.]* **29**, 874-880, July, 1950. 24 refs.

Comparative studies of nitrogen balance and of the metabolism of eight individual amino-acids were carried out on 3 normal subjects, 3 patients with ulcerative colitis, and one patient with regional enteritis. All patients showed an increased loss of nitrogen and amino-acids in the faeces, due to the loss of tissue fluids, exudate, and blood from the ulcerated bowel. Utilization of administered proteins was normal. In 3 patients the total non-protein amino-acid concentration in plasma increased, although the concentration of free amino-acids in plasma was normal. The occurrence of such a hyperpolypeptidaemia in other diseases is discussed.

P. Mestitz

### 34. The Effect on Nitrogen Balance and Plasma Protein Content of Vegetarian and Lacto-vegetarian Diets. (Das Verhalten der Stickstoffbilanz und der Bluteiweisskörper bei vegetabilischer und lacto-vegetabilischer Ernährung)

F. GROSSE-BROCKHOFF and H. J. HAASE. *Deutsches Archiv für Klinische Medizin [Dtsch. Arch. klin. Med.]* **197**, 378-392, 1950. 3 figs., 21 refs.

One of the authors, aged 25 years and normally weighing 65 kg., was kept under observation for a period of 397 days during which changes in nitrogen excretion, body weight, and blood protein level were determined, while the diet was altered so as to contain varying amounts of (a) exclusively vegetable protein, or (b) vegetable and milk proteins, the total energy content remaining fairly constant at 2,811 to 2,991 Calories daily. Nitrogen equilibrium was attained with a daily intake of 74 g. of purely vegetable protein and with one of 64 g. of mixed protein (44 g. milk and 20 g. vegetable). On changing from mixed protein to vegetable protein the weight increased, while the reverse change had the opposite effect on weight but caused the blood albumin level to fall. This is interpreted as indicating increased retention of water on changing from the mixed to the purely vegetarian diet. Larger increases in the consumption of milk protein caused the blood proteins to rise to the high value of 8 g. per 100 ml. An addition of 1 g. of cystine daily to the vegetarian diet had no effect on absorption or retention of protein. These findings, together with experience gained in the treatment of cases

of severe under-nutrition, indicate, in the authors' view that gross manifestations of protein deficiency, such as oedema, are found only when the protein deficiency is accompanied by a deficiency of energy; they also tend to support the old view that protein consumption should be at about the level of 1 g. per kg. body weight and that half of it should be animal protein.

H. E. Magee

### 35. Experimental Studies on Vitamin-D Poisoning. (Experimentelle Untersuchungen zur Vitamin-D<sub>2</sub>-Vergiftung)

G. SCHETTLER. *Zeitschrift für die Gesamte Experimentelle Medizin [Z. ges. exp. Med.]* **116**, 138-149, Aug. 7, 1950. 20 refs.

The toxicity of vitamin D, first investigated 22 years ago, has been re-examined by the author in respect of vitamin D<sub>2</sub>. The experiments were carried out on young, fully developed dogs and the lethal doses found in these investigations were in general lower than those found by previous workers. The well-known symptoms and signs of toxicity, such as anorexia, polydipsia, vomiting, diarrhoea, ataxia, and collapse appeared much more quickly after a single large dose of vitamin D<sub>2</sub> than after repeated smaller doses. Single oral doses of 4 to 5 mg. of a 6% oily, solution of crystalline vitamin D<sub>2</sub> per kg. body weight killed most of the dogs within 3 to 5 days. Some of them, however, survived the administration of even higher doses, but showed signs of intoxication for about 2 weeks. Intramuscular or subcutaneous administration of considerably higher doses (10 to 20 mg. per kg. body weight) resulted in delayed appearance of the signs and symptoms of toxicity. On the other hand, vitamin D<sub>2</sub> given intraperitoneally or intravenously, acted with approximately the same speed as by mouth.

Z. A. Leitner

### 36. The Relation in Man between Cholesterol Levels in the Diet and in the Blood

A. KEYS. *Science [Science]* **112**, 79-81, July 21, 1950. 1 fig., 9 refs.

This is a preliminary report on investigations into the relation between cholesterol intake and the serum cholesterol level in man. In 60 experiments on young men, the ingestion of 10 g. of cholesterol produced only trivial and transient increases in serum cholesterol content. Similarly studies on 482 clinically "normal" men over a period of more than 3 years showed that the serum cholesterol level is not significantly related to differences in habitual cholesterol intake over a range of about 250 to 800 mg. a day, while the reduction by one-half of the dietary cholesterol intake of 41 middle-aged men did not affect the serum cholesterol level.

However, the administration to hypertensive patients of the Kempner rice diet (which is cholesterol-free and almost fat-free) rapidly resulted in a marked fall in the serum cholesterol level; and in 2 cases of idiopathic hypercholesterolaemia the response was "even more dramatic than in normal men" [apparently the "normal men" referred to are the hypertensive patients, unless other studies were made which are not reported]. One of these 2 patients was then given vegetable fats (free of

cholesterol) and accumulated cholesterol rapidly. The author concludes that "the general picture, then, is that the blood [serum] cholesterol level is independent of the intake over a wide range, but that at zero intake it falls at a rate related to the previous level of cholesterol in the blood [serum]".

H. M. Sinclair

## NERVOUS SYSTEM

### 37. The Effects of Lesions in the Cingular Gyrus and Adjacent Areas in Monkeys

P. GLEES, J. COLE, C. W. M. WHITTY, and H. CAIRNS. *Journal of Neurology, Neurosurgery and Psychiatry* [J. Neurol. Neurosurg. Psychiat.] 13, 178-190, Aug., 1950. 10 figs., 31 refs.

Bilateral cingular-gyrus lesions with varying involvement of adjacent areas were made in 5 rhesus and 2 cebus monkeys, the animals being observed for 2 to 14 weeks after the operation. The animals became more tame and less aggressive and lost their sense of danger; 3 animals were continuously restless. These changes tended to disappear after a few weeks. The anterior part of area 24 was connected to areas 6, 8, 9, 10, 29, and to the anterior border of 4; most of these areas sent fibres back to the cingular gyrus. From the posterior part of the cingular gyrus, fibres were noted to pass into the anterior thalamic nucleus.

A. Schweitzer

### 38. The Position and Function of the Centre for Regulation of Blood Pressure. (Lage und Funktion des blutdruckregulierenden Zentrums in der Medulla oblongata (nach Befunden bei Poliomyelitis))

H. J. LÖBLICH. *Virchows Archiv für Pathologische Anatomie* [Virchows Arch.] 318, 211-233, 1950. 6 figs., 41 refs.

Hypertension combined with tachycardia in poliomyelitis, first described by Nordmann and Müller, occurs especially in cases in which life has been prolonged by treatment in an iron lung. The blood pressure, never exceeding double the normal, usually remains constant until death. In 6 cases of poliomyelitis the medulla oblongata and the diencephalon were examined at necropsy. In the 3 cases with hypertension, extensive destruction of ganglion cells had occurred in the formatio reticularis grisea on both sides at the level of the superior third of the olive, whereas in cases of respiratory paralysis the changes were localized on both sides to the level of the lower third of the olive. In cases with hypertension and paralysis of respiration both regions were affected, the lesions being separated by an unaffected zone. This shows that in man a centre for regulating the blood pressure, with vasodilator function, is situated in the formatio reticularis grisea of both sides, just above the respiratory centre. This finding is in accord with the results of experimental research on animals. Suspension of function of this centre on both sides leads apparently to predominance of the vasoconstrictor centres in the diencephalon and therefore to hypertension; suspension on one side only (observed in one case) does not cause hypertension; hence this centre, situated symmetrically

on each side, is a functional unit acting on both halves of the body. In 3 of the fatal cases of poliomyelitis severe cachexia was present.

O. Neubauer

### 39. Denervation Changes in Mammalian Striated Muscle

S. SUNDERLAND and L. J. RAY. *Journal of Neurology, Neurosurgery and Psychiatry* [J. Neurol. Neurosurg. Psychiat.] 13, 159-177, Aug., 1950. 15 figs., 47 refs.

The degenerative changes in the flexor carpi ulnaris, flexor carpi radialis, and pronator teres of the Australian opossum were studied 9 to 485 days after denervation. The general form of each muscle was fully retained in spite of its reduction in size and weight. The muscles did not become converted into an ill-defined fibrous sheet. Fibrillation was still seen after 485 days. The histological features of striated muscle fibres were retained. The weight loss of muscle after denervation was 30% after 29 and 50 to 60% after 60 days. From 120 days onward the weight loss remained constant between 60 and 80%. Individual muscle fibres atrophied more rapidly than the total weight loss indicated. There was no nuclear degeneration or proliferation, the majority of nuclei retaining their peripheral position. Striation (in spite of less intense staining) and muscle end-plates were visible. Only 2 specimens showed fibrous transformation of muscle fibres. The morphological characteristics of neuromuscular spindles were maintained, in spite of degeneration of the intrafusal fibre. The perimysial and endomysial connective-tissue content increased, this change being preceded by fibroblastic proliferation which reached a peak at 89 days. Endoneurial tubes were still visible after 485 days.

A. Schweitzer

### 40. Experimental Studies on the Origin of Vasodilator Nerves of the Limbs. Vasodilatation Induced in 5 Cases of Rupture of the Brachial Plexus in Man. (Recherches expérimentales sur l'origine des vaso-dilatateurs des membres. De la vaso-dilatation provoquée dans 5 cas d'arrachement du plexus brachial chez l'homme)

C. MENTHA. *Lyon Chirurgical* [Lyon chir.] 45, 168-180, Feb.-March, 1950.

In 5 cases of severe brachial-plexus injury the paralysis of the upper limb was complete or nearly so, and in each the limb was in the ultimate, vasoconstricted, cyanotic, "cold" phase. It was possible in every case to induce cutaneous vasodilatation in the affected limb by a variety of methods, namely, by intravenous injection of acetylcholine with a tourniquet in position and blocking the veins, by intradermal injection of histamine into an area of anaesthetic skin, or by injection of local analgesic into the stellate ganglion, both of the injured and of the contralateral side. The author, from a study of the results observed in these 5 cases, has come to regard paralytic and active vasodilatation as being the same. He postulates anew the existence of a continuous microscopic conducting network of vasoconstrictor fibres in relation to the major vessels of a limb, functioning as a whole and not necessarily being dependent on segmental contributions from peripheral nerves along its length.

M. R. Ewing

## Pharmacology and Therapeutics

### 41. The Influence of Amphetamine Sulfate upon the Acuity of the Sense of Taste for Sucrose and upon the Sensation Complex of Appetite and Satiety

A. J. AHOKAS, J. G. PAYNE, and F. R. GOETZL. *Permanente Foundation Medical Bulletin* [Permanente Fdn med. Bull.] 8, 107-112, July, 1950. 1 fig., 5 refs.

Experiments are described which demonstrate that amphetamine sulfate (10 mg.) is capable of simultaneously producing a decrease in acuity of the sense of taste for sucrose and a conversion of the sensation of appetite into one of satiety. The suggestion is made that the effectiveness of amphetamine sulfate in producing anorexia may be related to the depressant effect of this drug upon the sense of taste for sucrose and its depressant effect upon olfaction.—[Authors' summary.]

### 42. Evaluation of Curarizing Drugs in Man. II. Analysis of Response Curves and Effects of Repeated Administration of D-Tubocurarine, Dimethyl-D-tubocurarine and Decamethylene-bis(trimethylammonium Bromide). Antagonism to Curarizing Effects of D-Tubocurarine and Decamethylene-bis(trimethylammonium Bromide)

E. W. PELIKAN, K. R. UNNA, D. W. MACFARLANE, R. J. CAZORT, M. S. SADOVE, and J. T. NELSON. *Journal of Pharmacology and Experimental Therapeutics* [J. Pharmacol.] 99, 215-225, and 226-233, June, 1950. 1 fig., 39 refs.

The effects of D-tubocurarine chloride (DTC), dimethyl D-tubocurarine chloride (dimDTC) and decamethylene-bis(trimethylammonium bromide) ("C 10") on the grip strength, the vital capacity, and the time taken for 75% recovery of grip strength (t75) were determined in unanaesthetized volunteers breathing pure oxygen. The results were analysed statistically and it was shown that the order of potency of the drugs in each case was: (1) C 10, (2) dimDTC, (3) DTC. The threshold for effects on the respiratory muscles differed with each drug and also differed from the threshold for the peripheral muscles in each case. The "coefficient of safety", being the ratio of the dose required to reduce the vital capacity by 50% to that required to reduce the grip strength by 95%, was calculated for each drug and was shown to be lowest for C 10 and highest for dimDTC. In experiments in which repeated doses were given, tachyphylaxis to the curarizing effects of C 10 was observed in man, but not in animals. There was marked species variation in the response to curarizing drugs and the authors express the opinion that prediction of the quantitative responses in man on the basis of animal experiments is fraught with danger.

Pentamethylene-bis-(trimethylammonium iodide), given before the curarizing drug, failed to antagonize the action of C 10 in man and in the mouse and tended to potentiate the action of DTC in the latter. Neostigmine

was an effective antagonist of DTC in man and in the mouse, but was ineffective against C 10 in the latter. Large doses of C 10 in mice caused convulsions before paralysis became manifest, but it was shown that a prophylactic dose of 20 mg. of thiopentone soluble per kg. body weight prevented them and increased the LD 50 of C 10 by 42%. Forty-five minutes after a curarizing dose of DTC in man, C 10 was practically without effect.

P. A. Nasmyth

### 43. The Anticurare Activity of Tetraethyl-ammonium Ion in the Cat

C. J. KENSLEY. *British Journal of Pharmacology and Chemotherapy* [Brit. J. Pharmacol.] 5, 204-209, June, 1950. 6 figs., 18 refs.

### 44. Decamethonium ("C 10") and Regulation of the Blood Pressure. (Diiodure de décaméthonium (C 10) et homéostasie de la pression artérielle)

D. ATANACKOVIC. *Archives Internationales de Pharmacodynamie et de Thérapie* [Arch. int. Pharmacodyn.] 83, 277-287, 1950. 5 figs., 20 refs.

In earlier papers from Professor Heymans's laboratory at Ghent it has been shown that curarizing doses of tubocurarine, mephenesin, and "flaxedil" do not alter the blood pressure or the physiological mechanisms of blood-pressure regulation, although in higher doses tubocurarine does cause a fall in blood pressure and depresses the regulating mechanisms. It has now been shown, in dogs anaesthetized with morphine and chloralose, that decamethonium ("C 10") resembles tubocurarine in this respect. A curarizing dose, which first paralyses the thoracic respiratory muscles and later the skeletal muscles and diaphragm, does not lower the blood pressure nor alter the reflex carotid-sinus pressor response to bilateral occlusion of the common carotid arteries. Larger doses (3 mg. per kg.) of C 10 cause respiratory paralysis and a prolonged fall in blood pressure with abolition of the carotid-sinus pressor response, in spite of artificial respiration. Such a dose, 30 to 60 times the clinical curarizing dose, causes paralysis of autonomic ganglia. After premedication with morphine only, 2 mg. of C 10 per kg. does not cause hypotension or depression of the reflex. Subsequent injection of 90 mg. of soluble thiopentone, into a 16-kg. dog, also did not affect blood pressure or the reflex pressor response, but after the large dose of 260 mg. of thiopentone the reflex was much reduced. Following a completely curarizing dose of C 10, a decurarizing dose of pentamethonium ("C 5") caused a temporary fall in blood pressure, but there was a prolonged depression of the reflex pressor response.

Derek R. Wood

### 45. Decamethonium Iodide in Muscular Hypertonus

A. A. GUILD. *Lancet* [Lancet] 2, 251-252, Aug. 12, 1950. 3 figs., 3 refs.



46. **Studies on the Pharmacology and Toxicology of DL- $\alpha$ -1:3-Dimethyl-4-phenylpropionyloxy Piperidine** C. M. GRUBER, K. S. LEE, and C. M. GRUBER, JR. *Journal of Pharmacology and Experimental Therapeutics* [J. Pharmacol.] **99**, 312-316, July, 1950. 1 fig., 11 refs.

47. **A Comparison of the Actions of Meperidine, Nu-1196, Methadone, Morphine, Nu-2206, and Metapone upon the Intestine and Uterus**

C. M. GRUBER, K. S. LEE, and C. M. GRUBER, JR. *Journal of Pharmacology and Experimental Therapeutics* [J. Pharmacol.] **99**, 317-324, July, 1950. 6 figs., 9 refs.

48. **Intravenous Procaine: its Effect on the Human Electrocardiogram and on Cardiac Arrhythmias.** [In English]

A. I. SCHAFFER, R. STEINMAN, and D. SCHERF. *Cardiologia* [Cardiologia, Basel] **16**, 342-353, 1950. 2 figs., 8 refs.

One group of patients received an intravenous drip infusion of procaine hydrochloride in 0.1% solution in saline at a dosage ranging from 300 to 500 mg. in 8 to 30 minutes. A second group received an intravenous injection of a 1.0% solution in a dosage of about 100 mg. within 4 seconds. The effects on the electrocardiogram, blood pressure, respiration, and appearance of different symptoms were carefully observed. Procaine did not significantly influence auricular flutter and paroxysmal tachycardia: slight slowing of the rate indicated a direct action on the abnormal centres of stimulus formation. The appearance of abnormal extrasystolic stimulus formation under the influence of procaine in the doses given above suggests that it is dangerous to give larger doses in an effort to treat arrhythmias.

[It appears that the effect of intravenously injected procaine depends not only on the dosage but also to a great extent on the rate of administration. Procaine is destroyed rapidly in the blood, and hence large doses very near to the convulsive ones must be used.]

G. B. West

49. **Further Studies of the Effect of Ergonovine on the Coronary Circulation**

I. STEIN and J. WEINSTEIN. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] **36**, 66-81, July, 1950. 4 figs., 4 refs.

Ergonovine maleate is a substance which reduces the coronary circulation and hence may be used clinically to confirm the presence of coronary arterial insufficiency when symptoms are present but routine physical and electrocardiographic examination offers no confirmatory evidence. In a series of 66 tests on 30 patients with cardiovascular disease the intravenous injection of 0.2 to 0.6 mg. of ergonovine produced electrocardiographic alterations (S-T depression and T-wave inversion) and pain in all cases (15) in which a clinical diagnosis of anginal syndrome had been made. The pain was relieved by giving 0.65 mg. of nitroglycerin, while nitroglycerin administered simultaneously nullified the effect of ergonovine in previously positive cases, which suggests that the latter substance acts directly on the

coronary vessels, producing spasm. There were no significant pulse or blood-pressure changes during the test. No significant toxic effects were noted. The authors suggest that nitroglycerin be available whenever the test is carried out.

G. B. West

50. **Multiple-balloon Kymographic Recording of the Comparative Action of Oral Administration of Atropine, Tincture of Belladonna and Placebos on the Motility of the Upper Small Intestine in Man**

W. P. CHAPMAN, E. N. ROWLANDS, and C. M. JONES. *New England Journal of Medicine* [New Engl. J. Med.] **243**, 1-8, July 6, 1950. 6 figs., 13 refs.

An experiment is described in which the effect of the administration of atropine and belladonna upon small intestinal activity was investigated in 14 volunteer subjects. Four balloons were introduced simultaneously into the upper small intestine and the pressure within them recorded kymographically. As soon as the balloons were in a satisfactory position, either tincture of belladonna, 0.4 ml., or atropine, 0.04 mg., was given by mouth. The test was performed on each subject with one of the drugs and repeated with a placebo. Results were analysed according to three types of gut activity: (1) propulsive contraction as shown by serial responses in the balloon records; (2) total contractile activity as measured by the total area traced by the recording pens in a given time; and (3) tone, which was assumed to be responsible for the constant balloon pressure when no active contraction was taking place. In the control experiments administration of the inert placebo caused considerable diminution in propulsive contractions for about 4 hours, after a very variable latent period. The drugs, after a latent period averaging 25 minutes, caused a diminution in activity which was double that seen in the controls. This effect lasted for 2 hours, after which both drug and placebo had similar effects. The total contractile activity of the gut was diminished in a similar manner, though in this case the effect of the drugs was significantly greater than that of the placebo for 3 hours. Though the authors think that tone was usually somewhat diminished when the drugs were given, the effect was inconstant. In all cases the action of belladonna and atropine in equivalent doses was almost identical.

[This experiment has two unsatisfactory features: first, the use of balloons as a method of recording gut activity is subject to considerable criticism, this being particularly pertinent in the case of tonic pressures; and, secondly, the number of cases is inadequate.]

A. G. Parks

51. **Multiple Balloon Kymograph Recording of the Comparative Action of Morphine and Placebos on the Motility of the Upper Small Intestine in Man**

E. N. ROWLANDS, W. P. CHAPMAN, A. TAYLOR, and C. M. JONES. *Surgery, Gynecology and Obstetrics* [Surg. Gynec. Obstet.] **91**, 129-137, Aug., 1950. 5 figs., 13 refs.

Nine observations were made of the effect of morphine and of placebos, given subcutaneously, on the motility of the upper small intestine, either 2 or 7 balloons being

introduced into adjacent segments of the duodenum and upper jejunum.

Within 15 minutes of the injection of 10 mg. of morphine, spasm started in the duodenum and passed forward to the jejunum. The spasm lasted for about 15 minutes and was followed by further temporary increases in tone at intervals ranging from 10 to 25 minutes. This effect was followed up, and continued for between 4 and 5 hours in most cases. During the spasms, propulsive contractions were almost completely abolished. In the intervals between the spasms tone tended to be slightly decreased and propulsive contractions reappeared, but were less marked than in the pre-drug control period.

The injection of a placebo frequently produced a spasm about 15 minutes afterwards, which was associated with a striking temporary decrease in propulsive contractions. There was frequently only the one spasm, or at the most three spasms, in the space of 4 hours after a placebo had been given. Epigastric pain as a result of the intestinal spasms was noted in only one of the tests.

[That these intestinal spasms are capable of causing severe epigastric pain is claimed because of the case of a 54-year-old woman who suffered from increased epigastric pain when given codeine or morphine for biliary colic. It is apparently not widely known that morphine causes a rise in intrabiliary pressure, which aggravates this painful condition (Goodman and Gilman, *The Pharmacological Basis of Therapeutics*, p. 199. New York, 1941). There may be an initial relief of the pain due to the action of morphine on the higher centres, but subsequently the pain is often more severe, because the peripheral action causes biliary spasm. It does not seem permissible, therefore, to use this case to substantiate the possibility that the intestinal spasm caused by morphine may give rise to pain.]

P. A. Nasmyth

**52. Mechanism of the Hyperglycaemic Action of Acetylcholine, Morphine, and Nicotine.** (Mécanisme de l'action hyperglycémique de l'acétylcholine, de la morphine et de la nicotine)

G. VAN DEN HEUVEL-HEYMAN. *Archives Internationales de Pharmacodynamie et de Thérapie* [Arch. int. Pharmacodyn.] **83**, 386-416, 1950. 8 figs., bibliography.

Experiments were performed on rabbits, some of which had been adrenalectomized and then maintained by injections of deoxycortone acetate. In non-anaesthetized animals a hyperglycaemia lasting for at least 60 minutes is produced by doses of acetylcholine insufficient to cause convulsions, but the response is absent in animals anaesthetized with pentobarbitone. Neither atropine nor the adrenolytic compound, "SY-28", influences the hyperglycaemic effect of acetylcholine or adrenaline. The anticholinesterase drug, "Nu-683", can itself cause hyperglycaemia if given in high doses, while smaller doses potentiate the effect of acetylcholine. Tetraethylammonium prevents these effects unless the dose of acetylcholine is sufficient to cause convulsions. It also prevents the hyperglycaemic actions of morphine and nicotine. Adrenalectomy abolishes the hyperglycaemic effect of all three

compounds. It is concluded that the action of these substances is the result of increased liberation of adrenal hormone due to central or ganglionic stimulation.

Derek R. Wood

**53. Species Difference in Noradrenaline Content of Adrenal Glands.** (Artspezifische Unterschiede im Arteriengehalt des Nebennierenmarks)

P. HOLTZ and H. J. SCHÜMANN. *Archives Internationales de Pharmacodynamie et de Thérapie* [Arch. int. Pharmacodyn.] **83**, 417-430, 1950. 6 figs., 39 refs.

These workers at the Pharmacological Institute of the University of Rostock confirmed their finding that the adrenal glands of rabbits and guinea-pigs contain no noradrenaline, in contrast to glands from the ox, cat, pig, dog, and man. They tested gland extracts for effects on the blood pressure of the cat, on rabbit intestine, and on rat uterus. In gland extracts from rabbits and guinea-pigs activity was equal to that of a pure adrenaline solution on all three test objects. The physiological importance of the observations is discussed.

Derek R. Wood

**54. Promethazine ("Phenergan", "3277 R.P.") and the Schwartzman Phenomenon.** (Chlorhydrate de N-( $\beta$ -diméthylamino- $\beta$ -méthyléthyl) phénothiazine (3277 R.P. ou phénergan) et phénomène de Schwartzman)

J. J. REUSE. *Archives Internationales de Pharmacodynamie et de Thérapie* [Arch. int. Pharmacodyn.] **83**, 332-334, 1950. 7 refs.

In view of contradictory reports on the effects of antihistamine substances on the Schwartzman phenomenon, the author tested the effect of promethazine on this reaction in rabbits. By giving three intramuscular doses of promethazine (20 to 25 mg. per kg.) 30 minutes before the first injection of culture filtrate, 30 minutes to 6 hours before, and 2 to 6 hours after the later intravenous injection of filtrate, an adequate amount of antihistamine drug was injected. A moderate or strong reaction occurred in 10 of 12 control animals, and in 17 of 22 animals treated with promethazine. The technique does not allow of a more quantitative assessment of the result. No evidence was obtained suggesting a protective action of promethazine.

Derek R. Wood

**55. Comparison of the Anterior Pituitary-Adrenal Cortical Stimulating Effect of U.S.P. Epinephrine, Synthetic L-Epinephrine, and Nor-epinephrine**

L. L. MADISON. *Journal of Clinical Investigation* [J. clin. Invest.] **29**, 789-791, June, 1950. 1 fig., 21 refs.

**56. Experience with the New Anticoagulant, B.O.E.A.**

C. SOLOMON, H. J. MCNEILE, and R. LANGE. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] **36**, 19-22, July, 1950. 2 figs., 5 refs.

"B.O.E.A." ("tromexan") is bis-3 : 3'-(4-oxy-coumarinyl) ethyl acetate, a compound chemically similar to dicoumarol, but four times more soluble, more rapidly absorbed, more rapidly excreted, and of lower toxicity. It is administered orally, its dosage being determined, as

with dicoumarol, by its effect on the prothrombin time. The present investigation, in which 10 healthy volunteers and 25 patients [diagnoses not stated] received the drug, showed that (a) in the majority of patients an initial dosage of 1.5 to 1.8 g. was necessary to raise the prothrombin time, as estimated by the Quick method, above 25 seconds; (b) maintenance doses of 0.3 to 0.9 g. daily were necessary to maintain this therapeutic level; and (c) if the drug was given 8-hourly only one prothrombin-time estimation daily was necessary. In all cases the prothrombin time returned to normal within 24 hours of discontinuing the drug. No evidence of toxicity was found except in the case of one patient who had transient microscopic haematuria.

[It would appear that B.O.E.A. is a great advance, even over dicoumarol, in the treatment of thrombo-embolic disease. Being more soluble, it is more rapidly absorbed so that the delay in initial action is reduced. The number of cases treated is, however, small.]

G. B. West

#### 57. The Effect of Dicoumarol on the Erythrocyte Sedimentation Rate

R. H. WIER, J. C. EAGAN, and S. A. WOLFSON. *Annals of Internal Medicine* [Ann. intern. Med.] 33, 354-360, Aug., 1950. 4 figs., 11 refs.

The effect of the administration of dicoumarol on the erythrocyte sedimentation rate (E.S.R.) was studied in 3 patients with diseases not causing an increase in the E.S.R., and in 16 cases of acute myocarditis. In both groups an initial dose of 300 mg. of dicoumarol was given, followed by 200 mg. on the second day, subsequent doses being dependent on the blood prothrombin level, which was determined daily by Quick's method. The E.S.R. was determined (by Cutter's method) daily in the first group, twice weekly in the second.

No increase in E.S.R. was observed in the first group of patients despite a reduction in prothrombin level to as little as 17% of the normal. Nor was any correlation to be found between E.S.R. and blood prothrombin level in the patients with myocardial infarction, the E.S.R. in 6 cases returning to normal despite continued dicoumarol therapy, and its value in the other 10 cases being unaffected by fluctuations in the blood prothrombin level. Further support is thus provided for recent assertions that, contrary to earlier reports, the administration of dicoumarol in no way diminishes the value of the E.S.R. as a gauge of progress in such conditions as myocardial infarction.

D. I. Crowther

#### 58. The Diuretic Action of a Coumarin-mercurial Compound

S. SHAPIRO and M. WEINER. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] 36, 224-229, Aug., 1950. 2 figs., 6 refs.

"Mercumatilin", or "EN 564", a compound of theophylline with 8-(2'-oxymethyl-3'-methoxy)propyl-coumarin-3-carboxylic acid, is a new, chemically stable, organic mercurial diuretic which differs structurally from the commonly available cyclic mercurial diuretics in containing a bicyclic heterocyclic ring and in that the

mercurated allyl grouping is attached to a carbon atom instead of to a nitrogen atom. It was available to the authors in 2.0-ml. ampoules containing 278 mg. of the mercury-theophylline compound with a slight excess of theophylline. On testing with sodium sulphide, the solution was found to be free from ionizable mercury. Although a compound of coumarin, EN 564 did not give rise to any degree of hypoprothrombinaemia. Animal toxicity tests showed it to be no more toxic than the commonly used mercurial diuretics. The pH of the preparation was 7.25 and it was not locally irritating or unduly painful when given intramuscularly.

A clinical trial was performed on chronically-ill patients in the Goldwater Memorial Hospital, New York, including cases of chronic heart disease (rheumatic, arteriosclerotic, hypertensive, and syphilitic), cirrhosis of the liver, and kidney disease. The patients were receiving routine injections of "mercuhydrin" for the control of oedema, ascites, or both, and after a period of stabilization and observation of response the new mercurial was given, each patient receiving 2 to 20 injections of EN 564 alternating with injections of mercuhydrin at intervals of at least 2 days. New patients who had received no previous mercurial therapy or whose treatment had been inadequate showed the most marked response to both mercurial preparations, but were excluded from this study because of difficulty in comparing responses at different times. Patients with massive oedema were likewise excluded because of the more marked response in such cases to the first injection of a diuretic compared with subsequent injections.

A total of 105 intramuscular injections of 2.0 ml. of EN 564 were given to 19 patients. The average response of each individual patient to each preparation was determined by averaging the loss of weight within the 48-hour period following each injection. EN 564 produced a greater average diuresis than mercuhydrin, and statistical analysis of the correlated data showed that this difference was significant. No evidence of systemic toxicity was noted. Urinary examination showed no significant change in content of albumin, casts, or cells. In a selected group of cases no significant change was noted in blood urea nitrogen level or erythrocyte and leucocyte counts. The routine intramuscular administration of EN 564 alone since this study was completed has been effective and without incident.

N. R. W. Taylor

### CHEMOTHERAPY

#### 59. The Activating Effect of Calcium on a Bactericidal Substance for *Bacillus subtilis* in Human Serum

R. F. JACOX. *Journal of Experimental Medicine* [J. exp. Med.] 92, 101-111, Aug., 1950. 15 refs.

Although 100 sera from normal persons were generally without bactericidal activity on *Bacillus subtilis*, sera from patients in hospital for a variety of pathological conditions were sometimes very active in this respect. Furthermore, the level of bactericidal activity was closely related to the stress of the pathological process, but this stress was not necessarily related to such factors as fever



or leucocytosis. In patients who recovered from their illness, the bactericidal power of the serum tended to disappear during convalescence.

There is evidence that the inhibitory power is not due to a specific antibody, because it requires ionizable calcium for its activity; the addition of sodium salts of phosphoric, citric, or oxalic acid caused a loss of activity, which could be restored by the addition of ionized calcium. Similar concentrations of magnesium salts were without effect.

There is evidence that the bactericidal activity for *B. subtilis* described above is distinct from the classical bacteriolysin-complement mechanism of immunity. In view of the fact that other investigators have found that acute-phase sera from patients with a number of pathological conditions may possess bactericidal activity for micro-organisms not usually susceptible to bacteriolysin-complement, it is possible that the new mechanism depending on calcium may prove to be a third method of defence against bacterial invasion.

R. Hare

#### 60. Synergism and Antagonism as Displayed by Certain Antibacterial Substances

J. W. BIGGER. *Lancet [Lancet]* 2, 46-50, July 8, 1950. 5 refs.

This paper records the results of an investigation undertaken to determine the interaction of sulphathiazole, penicillin, streptomycin, chloramphenicol, boric acid, and *p*-aminosalicylic acid when tested *in vitro* in pairs against *Bacterium coli*. A synthetic medium was used and its pH adjusted to 7.5. The results are summarized in the following table:

	Sulphathiazole	Penicillin	Streptomycin	Chloramphenicol	Boric Acid	<i>p</i> -Aminosalicylic Acid
Sulphathiazole	—	S	S	AS	A	AS
Penicillin	S	—	S	S	AS	S
Streptomycin	S	S	—	S	S	AS
Chloramphenicol	S	S	S	—	S	S
Boric acid	A	S	S	S	—	S
<i>p</i> -Aminosalicylic acid	S	S	S	S	S	—

To be read downwards, not across.  
S=Synergism. A=Antagonism.

Antagonism was demonstrated in five combinations, but only in the case of boric acid and sulphathiazole was each constituent antagonistic to the other. The only other marked and permanent antagonisms were those of *p*-aminosalicylic acid to sulphathiazole and of boric acid to penicillin. In the case of some combinations both antagonism and synergism were found at different concentrations of the antibiotics. In two cases of antagonism (chloramphenicol to sulphathiazole and *p*-aminosalicylic acid to streptomycin) the antagonism which was obvious for the first day or two was replaced by synergism within 3 days.

The theoretical and practical importance of these findings are discussed. The author's general conclusion is that "as regards the six substances investigated, the synergism which, with a single exception, occurs between

them might be of considerable value and the antagonism which has been demonstrated in a few cases is very unlikely ever to represent a real danger".

A. W. H. Foxell

#### 61. The Influence of a New Benzoic Acid Derivative on the Metabolism of *para*-Aminosalicylic Acid (PAS) and Penicillin

W. P. BOGER, J. O. BEATTY, F. W. PITTS, and H. F. FLIPPIN. *Annals of Internal Medicine [Ann. intern. Med.]* 33, 18-31, July, 1950. 7 figs., 18 refs.

It has been found that "benemid", *p*-(di-*n*-propylsulphamyl)-benzoic acid, has the property of enhancing the concentrations of both penicillin and *p*-aminosalicylic acid (PAS) in plasma. Single oral doses of 1 and 2 g. were effective in doubling the plasma concentration of penicillin and PAS for periods of up to 8 hours. Most of the patients (50 were studied) received "benemid" for no longer than 2 or 3 days, but some received the compound for 40 days in an oral daily dose of 1.5 g. without toxic symptoms.

R. Wien

#### 62. Benemid and Carinamide: Comparison of Effect on *para*-Aminosalicylic Acid (PAS) Plasma Concentrations

W. P. BOGER, F. W. PITTS, and M. E. GALLAGHER. *Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.]* 36, 276-282, Aug., 1950. 5 figs., 13 refs.

Carinamide (caronamide) has been used to enhance plasma penicillin concentrations after administration of the antibiotic by delaying its excretion, and has also been found to enhance the plasma concentration of *p*-aminosalicylic acid (PAS) 2 to 4 times. The dose required (24 g. a day) is, however, inconveniently large when superimposed on a large daily dose (12 to 16 g.) of PAS, and the two together often cause nausea and vomiting. Preliminary trials suggest that "benemid" (*p*-(di-*N*-propylsulphamyl)-benzoic acid) may be more suitable for the purpose, as it appears to increase the plasma concentration of penicillin 2 to 5 times and of PAS 2 to 4 times in daily oral doses of 2 g. only.

The authors, working at the Philadelphia General Hospital, have compared the effects of carinamide and benemid on the plasma PAS level reached after the administration of 2 g. or 4 g. of PAS orally to patients with no evidence of renal, hepatic, or cardiac disease. In 5 patients the injection of 3 g. of carinamide intravenously in 15% solution after a single dose of 2 g. of sodium PAS increased by 2 to 4 times the plasma concentration of PAS as compared with the level reached when PAS was given alone, the effect lasting up to 2 hours, while when 2 g. of sodium PAS and 3 g. of carinamide were given 3-hourly, the value maintained was increased two-fold. In 6 patients given 3 g. of carinamide 3-hourly for 24 hours before the administration of a single dose of 4 g. of sodium PAS, the plasma PAS concentration 4, 6, and 8 hours thereafter was 2 to 4 times greater than when no carinamide had been given. When the same 6 patients were given 0.5 g. of benemid 6-hourly by mouth for 24 hours before the same dose of PAS, a higher plasma PAS level was observed in 2, the same level in 2, and a slightly lower level in the remaining

2 patients 4, 6, and 8 hours later, as compared with the levels after premedication with carinamide. On average, therefore, the enhancing effect of a daily dose of 2 g. of benemid was equivalent to that of 24 g. of carinamide.

Malcolm Woodbine

## ANTIBIOTICS

### 63. The Susceptibility of Pleuropneumonia-like Organisms to the *in vitro* Action of Antibiotics: Aureomycin, Chloramphenicol, Dihydrostreptomycin, Streptomycin, and Sodium Penicillin G

P. R. LEBERMAN, P. F. SMITH, and H. E. MORTON. *Journal of Urology* [J. Urol.] **64**, 167-173, July, 1950. 1 fig., 29 refs.

In experiments *in vitro* streptomycin was found to be the most effective antibiotic against 12 strains of pleuropneumonia-like organisms (PPLO), the majority being inhibited by 0.1  $\mu$ g. per ml., although two required 15  $\mu$ g. per ml. Dihydrostreptomycin was effective only against 6 out of 12 strains at concentrations of 15 to 50  $\mu$ g. per ml.

Some strains were inhibited by chloramphenicol and aureomycin at concentrations of 5 to 40  $\mu$ g. per ml., but 3 strains were not inhibited by 200  $\mu$ g. of aureomycin per ml. or 100  $\mu$ g. of chloramphenicol per ml. Growth of PPLO appeared to be enhanced by these two antibiotics. Crystalline sodium penicillin G had no effect even at a concentration of 1,000 units per ml. The L forms may be bacterial variants resistant to the action of many antibiotics and chemotherapeutic agents.

A. W. H. Foxell

### 64. *In vitro* Sensitivity of Pathogenic Enteric Bacteria to Various Antibiotics

G. G. JACKSON, T. M. GOCKE, H. S. COLLINS, and M. FINLAND. *Journal of Infectious Diseases* [J. infect. Dis.] **87**, 63-70, July-Aug., 1950. 3 figs., 1 ref.

One-third of 164 strains of pathogenic enteric bacteria were isolated from stools or blood of patients acutely ill with enteric infections. The antibiotics tested against them included crystalline penicillin G (potassium salt), streptomycin-CaCl<sub>2</sub> complex, bacitracin (34 units per mg.), polymyxin D hydrochloride, polymyxin B hydrochloride, crystalline "chloromycetin" (chloramphenicol), crystalline aureomycin hydrochloride, neomycin sulphate (173 units per mg.), and crystalline terramycin hydrochloride.

The sensitivity of the strains was assayed by a plate-dilution method with heart-infusion agar of pH 7.2 and serial two-fold dilutions of the antibiotics. Each segment of the plate was streaked with 1 loop (10<sup>7</sup>) of organisms, and the plates were examined after 24 and 48 hours' incubation at 37° C. The 164 strains were tested against 7 of the antibiotics and, in addition, 11 were tested against neomycin and terramycin. The 35 strains of *Salmonella typhi* included 15 phage types, 55 of the other salmonellae included 1 or more of 22 types, while 36 types and sub-types were included in the 74 strains of shigellae.

All the strains were most sensitive to the polymyxins (0.8 to 3.1  $\mu$ g. per ml.); chloramphenicol (0.8 to 12.5  $\mu$ g. per ml.) came next, with penicillin (1.9 to 60.0  $\mu$ g. per ml.) of equal effectiveness against most salmonellae, especially *Salm. typhi*, followed by aureomycin (3.1 to 50.0  $\mu$ g. per ml.) and streptomycin (3.1 to 200.0  $\mu$ g. per ml.). Bacitracin (3,000 to 24,000  $\mu$ g. per ml.) was the least effective. There was no definite correlation between sensitivity of any given strain to one antibiotic and its sensitivity to the others. No correlation was evident between type and sensitivity.

Malcolm Woodbine

### 65. Use of Penicillin O in Patients Hypersensitive to Penicillin G

I. F. VOLINI, W. H. SHALES, and O. FELSENFELD. *Journal of the American Medical Association* [J. Amer. med. Ass.] **143**, 794-797, July 1, 1950. 19 refs.

Several workers have reported that persons hypersensitive to penicillin G may show no reaction to some of the biosynthetic penicillins. One of these is allylmercaptomethyl penicillin, or penicillin O. The minimum inhibitory concentrations of penicillin O for Gram-positive cocci are the same as, or double, those of penicillin G. Furthermore, penicillin O was found to be less toxic and less irritating than penicillin G when injected subcutaneously into mice. The absorption and excretion curves of these two penicillins are essentially the same.

Penicillin O was administered to 57 patients who had clinical symptoms of hypersensitivity to penicillin G within a preceding period of not more than 200 days. Twenty of them had upper respiratory infections, and were given inhalations of penicillin-O dust, 100,000 units every 4 hours for 7 days. All recovered without complications and showed no allergic phenomena. In 23 cases of tonsillitis and pharyngitis due to  $\beta$ -haemolytic streptococci the patient received 10 troches containing 3,000 units of penicillin O daily for 3 days. The results were excellent in 15, good in 5, and poor in 3 cases. Fourteen patients received courses of injections of penicillin O, following which penicillin G was given and was well tolerated. It appears that penicillin O had a desensitizing effect. Seven of the cases are reported in detail and a further 7 in tabular form. In every case penicillin O was as effective as penicillin G.

A. W. H. Foxell

### 66. Experimental Neutralization of Tetanus Toxin by Penicillin G. (Neutralización experimental de la toxina tetánica por medio de la penicilina G)

A. E. IMBRIANO. *Revista Médica de Rosario* [Rev. méd. Rosario] **40**, 19-31, Jan.-Feb., 1950. Bibliography.

### 67. Studies in Penicillin Formation

R. P. COOK and M. B. BROWN. *Proceedings of the Royal Society of Edinburgh. B* [Proc. roy. Soc. Edinb., B] **64**, 137-171, 1949-50. 6 figs., bibliography.

### 68. On Penicillin Inactivators and Susceptibility of Micro-organisms to Penicillin

J. W. CZEKALOWSKI. *Edinburgh Medical Journal* [Edinb. med. J.] **57**, 281-304, July, 1950. Bibliography.

# 69. Evaluation of Oral, Intravenous, and Intramuscular Aureomycin and the Correlation between the *in vivo* and *in vitro* Activity

M. KLEIN, S. E. SCHORR, S. TASHMAN, and A. D. HUNT. *Journal of Bacteriology* [J. Bact.] **60**, 159-169, Aug., 1950. 3 figs., 7 refs.

A type-I pneumococcus was used throughout these studies. Growth of 0.1 ml. of a 1 in 100 dilution of an 18-hour broth culture of this strain was inhibited by 0.04 unit of penicillin and 0.12 µg. of aureomycin after 18 hours' incubation at 37° C. Drug action was determined in experimental infections in white mice given an intraperitoneal injection of approximately 10,000 MLD. A single intramuscular injection of 1 mg. of aureomycin was far more effective than one of 1 mg. of penicillin. This is related to the fact that aureomycin is more slowly absorbed than penicillin from the site of the injection, and therefore a therapeutic level in the blood is maintained for a longer period. No prolonged effect was obtained with large oral doses or intravenous injections of aureomycin.

The concentrations of aureomycin used in this study were very large, for 0.5 mg. of aureomycin injected into a 20 to 22 g. mouse is equivalent to a dose of 1.5 g. of aureomycin for an adult. Since intramuscular injections of 250 mg. of aureomycin are associated with considerable pain, it is not suggested that this form of therapy is feasible in human subjects.

The concentration of aureomycin required to inhibit growth *in vitro* of a type-I pneumococcus after 18 hours' incubation at 37° C. is 5 to 10 times greater than the concentration required to inhibit growth *in vivo*.

A. W. H. Foxell

# 70. Absorption and Excretion of Terramycin in Humans: Comparison with Aureomycin and Chloramphenicol

C. A. WERNER, V. KNIGHT, and W. McDERMOTT. *Proceedings of the Society for Experimental Biology and Medicine* [Proc. Soc. exp. Biol., N.Y.] **74**, 261-267, June, 1950. 2 figs., 5 refs.

Terramycin is an antibiotic produced by a species of *Streptomyces* and has been found to be active against a number of bacteria *in vitro* and *in vivo*. It was used in these experiments as the amphoteric base and as the hydrochloride, its absorption and excretion after oral administration being compared with those of aureomycin hydrochloride and chloramphenicol. The maximum serum concentrations attained after oral doses of 50 mg. per kg. body weight were 25 to 50 µg. per ml. for chloramphenicol, 12 to 16 µg. per ml. for terramycin, and 3.3 to 12.5 µg. per ml. for aureomycin. In the cerebrospinal fluid terramycin levels of up to 0.7 µg. per ml. were obtained, but they bore no direct relationship to the serum level. In 5 patients who received aureomycin none was found in the cerebrospinal fluid, even with a serum concentration of 7.6 µg. per ml. In 19 determinations on 7 patients who were receiving 25 to 50 µg. of chloramphenicol per kg., the cerebrospinal fluid level ranged from 4 to 50 µg. per ml. The urinary concentration of all 3 drugs varied over a wide range

after single doses of 25 or 50 mg. per kg., in some cases high concentrations being maintained for 24 hours.

A. W. H. Foxell

# 71. Clinical Observations on Terramycin

F. G. BLAKE, G. J. FRIOU, and R. R. WAGNER. *Yale Journal of Biology and Medicine* [Yale J. Biol. Med.] **28**, 495-507, July, 1950. 6 figs., 4 refs.

This paper records the results of treatment with terramycin of 15 patients with various infections. Terramycin hydrochloride was given orally in all cases. Various dosage schemes were employed, but treatment usually consisted of an initial dose of 1 g. repeated 4-hourly for 3 doses, followed by 3 to 6 g. a day in 3- or 4-hourly doses. Among the conditions in which good results were obtained were pneumococcal lobar pneumonia and infections due to staphylococci, *Streptococcus viridans*, *Strep. faecalis*, some strains of *Bacterium coli*, *Bacillus mucosus capsulatus*, *Proteus vulgaris* and Vincent's organisms. In 2 cases of subacute bacterial endocarditis the response was good, but relapse occurred as soon as treatment was stopped. The only toxic effects encountered were nausea, vomiting, and diarrhoea, which occurred in 12 of the 15 cases, but were troublesome in only 3.

A. W. H. Foxell

# 72. Antimicrobial Properties of Neomycin

S. A. WAKSMAN, E. KATZ, and H. LECHEVALIER. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] **36**, 93-99, July, 1950. 1 fig., 11 refs.

Neomycin is described as "an antibiotic substance produced by a strain of *Streptomyces fradiae* (No. 3535)". It is basic, water-soluble, heat- and microbe-resistant, and is active against many Gram-positive and Gram-negative bacteria and acid-fast bacteria, but not against fungi or true viruses. The authors report the preparation of an identical antibiotic from another strain (No. 3554) of the same organism. A comparative description of the characteristics of the two strains is given, with photomicrographs. A "factor X", consisting of an antibacterial factor, not yet fully recognized, and an antifungal factor, fradycin, are also removed from the cultures during the extraction of neomycin. Tabulated results are given showing the antibiotic activity *in vitro* of cultures of both strains against 7 organisms, and of neomycin itself against 24 Gram-positive and 24 Gram-negative bacteria, and against *Borrelia recurrentis*, *Leptospira icterohaemorrhagiae*, *Entamoeba histolytica*, *Trichomonas vaginalis*, fungi, viruses, and trypanosomes.

Neomycin is both bacteriostatic and bactericidal in action. In solution it was stable at room temperature for 24 hours within a pH range of 1.5 to 12.0. At pH 2.0 there was no loss of activity on heating for 10 minutes at 60° and 100° C., but there was a 40% loss of activity on heating at 120° C. for 10 minutes at pH 1.0, or pH 10.0. A solution of 50 units of neomycin incubated with 1 to 10 mg. of cysteine at pH 7.0 at room temperature for 3 to 24 hours was only slightly inactivated, but 1 mg. of cysteine added to an agar plate containing neomycin in a concentration of 2 units per ml.



caused partial inactivation. Neomycin was not inactivated by non-toxic concentrations of hydroxylamine, but its potency was reduced by nucleic and oleic acids. The effect of changes in the glucose and salt concentration of the medium and its reaction on the extent of the zone of inhibition produced by neomycin is emphasized. Later preparations of neomycin were more toxic than earlier preparations, the LD 50 for mice ranging from 1,000 to 1,500 units by subcutaneous or intraperitoneal injection, and about 200 to 300 units intravenously. Repeated injections were better tolerated. Preliminary studies in experimental animals indicate that neomycin is active *in vivo* against many bacteria, including the tubercle bacillus, that it has a high therapeutic index, and that it is of clinical value in treating a number of infections.

P. B. Marshall

**73. Use of Chloromycetin in Infections. I. In Non-bacterial (Atypical Undifferentiated) Respiratory Infections** P. COHEN and R. SCHWARTZ. *Journal of Pediatrics* [J. *Pediat.*] 37, 23-36, July, 1950. 6 figs., 20 refs.

A series of cases of acute respiratory infection were treated with chloramphenicol ("chloromycetin"). At first the oral dose used was 50 mg. per kg. per day, but it was soon found that better results were obtained with a dose of 100 mg. per kg. per day until the temperature subsided, followed by 50 mg. per kg. until the temperature had been normal for 4 days. An initial dose of 50 mg. per kg. per day divided into two or three doses given at hourly intervals was used in several cases. Because a solution causes nausea and vomiting the drug was given in capsules when possible, but for younger children it was mixed with chocolate or sweet cherry or raspberry syrup. With the doses used no toxic effects were encountered.

The diseases treated in this investigation were divided into three groups: (1) acute undifferentiated (abacterial) respiratory disease; (2) acute undifferentiated (virus) laryngo-tracheo-bronchitis; (3) atypical or abacterial pneumonia. There were no pathogens in the nasopharyngeal or tracheo-bronchial secretions or exudates in any of these cases. Influenza antibodies were found in several of the cases which responded to treatment, but the titre was so low as to indicate that the infections were not influenzal in origin. The leucocyte count was low, with a lymphocytosis rather than a polynucleosis. Only if these criteria of abacterial infection were satisfied and if there was failure of response to penicillin, or sulphonamides with penicillin, was chloramphenicol administered.

Eight patients of the first group were treated. They suffered from fever, headache, and malaise, with signs of involvement of the upper respiratory tract, but negative pulmonary findings. In 2 cases in which there was hyperpyrexia the temperature fell to normal in 24 to 48 hours. In other cases where there had been a persistently high temperature over a period of weeks this became normal in 48 hours, but the infection of nose and throat and the cough persisted for some days. This may have been due to inadequate dosage.

In the second group 7 cases were treated. They all had signs of tracheo-bronchitis and with the exception of one infant had no pulmonary infiltration. The absence

of significant pathogens suggested that these were cases of virus croup. With chloramphenicol the laryngeal symptoms and cough lessened considerably and the breathing became easier. The general impression was that the drug acted favourably, and that with the increased dosage more decisive results will be obtained.

In 11 cases of atypical pneumonia striking results ensued, with a precipitous drop in temperature and rapid improvement of the clinical picture. The physical findings disappeared in a few days. One infant developed suppurative otitis media whilst convalescent from pneumonia. This secondary infection responded to penicillin therapy, which had been useless at the onset of the original illness. Such cases suggest that combined antibiotic therapy may prove useful. Chloramphenicol was also found by the author to be useful in cases of congenital heart disease complicated by pulmonary infection of an atypical nature.

The authors state that "in view of the greater range of therapeutic efficiency of chloromycetin, which affects bacteria as well as filterable agents, it seems to us that the therapeutic agent of choice in acute respiratory infections of undetermined origin, in the absence of an influenza epidemic or a common cold, should be chloromycetin, particularly if the bacteriology of the respiratory tract has not been determined".

B. S. P. Gurney

**74. Tolerance and Effects of Lupulon in Man**

S. M. FARBER, J. M. MASTEN, H. H. ANDERSON, R. W. GENTRY, and Y. C. CHIN. *Diseases of the Chest* [Dis. *Chest*] 18, 10-15, July, 1950. 6 refs.

"Lupulon", a derivative of the soft resins of hops, was isolated and analysed in Germany in 1916 and 1925. The authors, working in various departments at the University of California, collaborated to investigate its effect against tuberculosis. *In vitro*, lupulon inhibits growth of tubercle bacilli in solutions of Dubos medium containing concentrations of the drug up to 1 in 40,000. In white mice infected intravenously with tubercle bacilli the number of organisms found in various organs is reduced. Given in 9 cases of moderately advanced pulmonary tuberculosis and one case of minimal disease the drug appeared to reduce the amount of sputum in 3 cases, render negative the sputum in 3 cases, and cause radiological improvement in 1 case. Although extensive laboratory investigations convinced the authors that this drug is of low toxicity, only 6 out of 10 patients were able to complete the 3-month course, anorexia, nausea, diarrhoea, and cramps compelling discontinuation in 4 cases.

[The authors consider that lupulon merits further study, but the results so far are not promising.]

J. Robertson Sinton

**75. Bongkreik Acid, a New Antibiotic.** [In English]

A. G. VAN VEEN. *Documenta Neerlandica et Indonesica de Morbis Tropicis* [Docum. neerl. indones. *Morb. trop.*] 2, 185-188, June, 1950. 2 figs., 6 refs.

A highly unsaturated fatty-acid-like substance is formed by a bacterium which can be isolated from coconut press-cake or grated fresh coconut. As a result of

the growth of the bacterium in these foodstuffs, known as "bongkreks", poisoning by bongkreks has long been recognized as not uncommon in Central Java. The toxicity of bongkreks acid for human beings and animals is due to its action on the liver and other tissues, which are unable to form glycogen. This failure is followed by hypoglycaemia which is not counteracted by intravenous injection of glucose. At the same time the blood lactic-acid content is greatly increased, as are the amino-acid and guanidine content of blood. Inorganic phosphate content of the blood is usually increased.

The whole picture of bongkreks poisoning closely resembles that of synthalin intoxication; 0.5 mg. is a lethal dose for pigeons. The provisional formula is  $(C_{11}H_{16}O_3)_x$  where  $x$  is probably 2; the acid is markedly labile. The acid has a very marked inhibitory action on *Staphylococcus aureus*, but not on Gram-negative bacteria. It also has an antibiotic effect on yeasts and on certain fungi such as *Penicillium glaucum* and *Rhizopus oryzae*. In nature it seems that there is a degree of antagonism between the growth of the bacterium and the fungus. Pieces of bongkreks which are totally covered by *Rhizopus* never cause poisoning.

G. M. Findlay

#### 76. A New Streptomycin

R. G. BENEDICT, F. H. STODOLA, O. L. SHOTWELL, A. M. BORUD, and L. A. LINDENFELSER. *Science [Science]* **112**, 77-78, July 21, 1950. 11 refs.

See also Section Respiratory Disorders, Abstract. 248

### TOXICOLOGY

#### 77. Treatment of Choice in Barbiturate Poisoning. Series of Twenty-nine Cases of Barbiturate Poisoning Treated with Pentylenetetrazole ("Metrazol") and Supportive Therapy

A. W. JONES, J. DOOLEY, and J. R. MURPHY. *Journal of the American Medical Association [J. Amer. med. Ass.]* **143**, 884-888, July 8, 1950. 17 refs.

Although picrotoxin is generally stated to be the drug of choice in barbiturate poisoning, it is admittedly somewhat dangerous if incorrectly employed. The authors sought to devise a safer and equally efficient method of treatment with leptazol. It consists in the immediate intravenous injection of 5 ml. of the [presumably 10%] solution, followed by 10 ml. in 15 minutes unless reflexes return. Thereafter 20 ml. is given intravenously every 30 minutes until the reflexes return. Small doses are given intramuscularly afterwards until full consciousness is restored.

Of 29 patients treated 13 were completely comatose and without reflexes when admitted. Of these 3 died, 2 from acute heart failure and one from bronchopneumonia, after recovering full consciousness. One of these had had only picrotoxin administration as treatment. The volume of leptazol solution administered varied from 2.5 ml. in an infant to 304 ml. in a man of 58 who had taken barbitone. [From the figures

given, it does not seem that the exact details of treatment advocated were followed, as in one case only 5 ml. of leptazol was given although consciousness was not restored for 72 hours, while in another case consciousness returned in 5 hours after a total of 130 ml.]

The remaining 16 patients all had intact light and corneal reflexes on admission. Five were treated with leptazol, and 11 with other drugs, chiefly nikethamide with or without picrotoxin. Curiously, the last group contained all but one of those who had taken phenobarbitone, a barbiturate with prolonged effect, while the great majority of the other 18 had taken "seconal" (sodium propylallylbarbiturate) or pentobarbitone, both drugs with a short-lived effect.

Reginald St. A. Heathcote

#### 78. Therapy of Acute Barbiturate Poisoning: Report of Three Cases

M. ROCHE, L. C. WYNNE, and D. M. HASKINS. *Annals of Internal Medicine [Ann. intern. Med.]* **33**, 73-82, July, 1950. 3 figs., 47 refs.

Three patients almost dead from about double the usual suicidal dose of barbiturate were treated successfully, not by administration of picrotoxin which the authors dislike and distrust, but by supportive measures such as gastric lavage, artificial respiration in a Drinker or similar machine, administration of oxygen, cardiac and respiratory stimulants, and antibacterial drugs combined, if necessary, with the evacuation of mucus from the bronchi by aspiration.

G. F. Walker

#### 79. The Effect of Alcohol on the Renal Excretion of Water and Electrolyte

M. B. STRAUSS, J. D. ROSENBAUM, and W. P. NELSON. *Journal of Clinical Investigation [J. clin. Invest.]* **29**, 1053-1058, Aug., 1950. 6 figs., 19 refs.

Experiments were carried out on 3 healthy adults, 147 ml. of 86 proof whisky (50 g. of absolute alcohol) being taken 5 hours after a meal. This caused an increased urinary excretion of water, without a corresponding increase in electrolyte excretion. Pure ethyl alcohol, given intravenously, had similar effects. During the diuresis the endogenous creatinine clearance was unaltered. The diuresis could be inhibited by the simultaneous administration of pitressin. The ingestion of a quantity of sodium chloride together with the whisky had a similar inhibitory effect. It appears that the diuresis caused by alcohol is due to some action of that drug on the supraoptico-hypophyseal mechanism.

P. Mestitz

#### 80. Toxic Effects in Animals and Man after Tetraethylammonium Bromide

A. J. P. GRAHAM. *British Medical Journal [Brit. med. J.]* **2**, 321-322, Aug. 5, 1950. 10 refs.

Tetraethylammonium bromide in 10% solution was given intramuscularly in doses of 2.5 mg. per kg. half-hourly for from 2½ to 5 hours to a series of 20 dogs. The dosage was just not large enough to cause a fall in blood pressure of more than 10 mm. Hg. It is shown by comparison with doses in man on a weight

basis that each individual dose is well on the safe side, but that the total amount is twice or thrice that normally given to man. Toxic effects appeared in 7 of the 20 dogs, beginning 2 to 3½ hours from the start of the experiment. [The figures for dosage are not clear, because only the total amounts given to this point, not those per kg., are stated. Further, figures for corresponding amounts for a 70-kg. man are given as 475 to 1,200 mg. (or 6.8 to 19.1 mg. per kg.), while from the description of the experiment it would seem that the dogs were given from 12.5 to 20 mg. per kg.] The signs of poisoning began with paralysis of the intercostal muscles and irregular movements of the diaphragm, lessened both in strength and frequency. Cyanosis and other signs of anoxia appeared. In 2 of the 7 dogs, after administration ceased, recovery began and was apparently complete in about 1½ hours. The remaining 5 [7 in the summary] died [though it is not clear whether administration of the drug had stopped or not]. In 3 [5 in the summary] death occurred in from 15 to 60 minutes from diaphragmatic paralysis, while in the other 2 sudden respiratory failure, thought to be central in origin, was the cause of death.

In 6 out of 7 subjects given tetraethylammonium bromide intravenously in doses of 250 to 300 mg. over 2 to 4 minutes, no toxic effects were seen. In the seventh, a woman of 22 given 300 mg., a curariform paralysis appeared. She became drowsy and unable to speak. There was loss of power in the muscles of the neck and arm, and intercostal respiration ceased. The movements of the diaphragm, on the other hand, were increased in size and frequency. The drowsiness became deeper, the pupils were somewhat dilated, with loss of the light reflex, and there was increased blood flow in the hand, with a slight rise in blood pressure. Within an hour recovery had begun and was complete in about 2 hours. Attention is drawn to the similarity of the effects of this drug in man and in animals, and to the danger of curariform poisoning during its use in man.

Reginald St. A. Heathcote

#### 81. The Toxic Effects in Man of the Anticholinesterase Insecticide Parathion (*p*-Nitrophenyldiethyl thionophosphate)

D. GROB, W. L. GARLICK, and A. M. HARVEY. *Bulletin of the Johns Hopkins Hospital* [Bull. Johns Hopk. Hosp.] 87, 106-129, Aug., 1950. 1 fig., 13 refs.

The toxic effects caused by parathion are described in 6 fatal, 4 severe, and 30 moderate cases of poisoning. Of the 6 fatal cases, 3 were in persons engaged in its manufacture and 3 in persons using the substance. Appearance of symptoms was often delayed for several hours after the last exposure to parathion. These began with anorexia and nausea, followed by parasympathetic effects resembling those of muscarine. There were also muscular fasciculations in the eyelids and tongue, and signs of central nervous intoxication going on to convulsions, coma, and death. The cholinesterase activity of the plasma was reduced in the severe cases to 5% of the normal, and that of the erythrocytes to 11 to 22%. It is suggested that the severity of the nervous effects is associated with the great lipid solubility of this

compound. The best results were obtained by treatment with atropine, of which large doses (2 mg. per hour) are tolerated. Convulsions can be controlled by ether or a barbiturate; curare and morphine are harmful.

V. J. Woolley

#### 82. Toxicity of Carinamide. A Review of 1,997 Patients

W. P. BOGER and J. W. CROSSON. *American Journal of Medicine* [Amer. J. Med.] 9, 35-43, July, 1950. 39 refs.

The authors have analysed the toxic symptoms occurring in a total of 1,997 patients—422 of their own cases, the remainder being derived from the literature or reported personally to the authors—to whom carinamide was administered together with penicillin in a wide variety of infections. The drug was given orally in all but 47 cases, and the dose in 85% was 1.5 to 4 g. every 3 to 4 hours for 1 to 14 days. Toxic reactions included nausea (243 cases), vomiting (110 cases), rashes (37 cases), drug fever (24 cases), proteinuria (19 cases), and, very rarely, other transient and mild discomforts. The risks of renal damage are held to be exaggerated and the claim is made that carinamide is but mildly toxic. [The newer prolonged-action penicillins have rendered discussions on the toxicity of carinamide largely academic.]

Henry Cohen

#### 83. Use of Ergot Preparations in Migraine

M. FUCHS and L. S. BLUMENTHAL. *Journal of the American Medical Association* [J. Amer. med. Ass.] 143, 1462-1464, Aug. 26, 1950. 13 refs.

It is generally thought that patients with migraine are unusually tolerant to ergot derivatives. Two cases presenting serious toxic symptoms are therefore reported. In the first, in a woman of 48, relief of migraine had been obtained on all occasions over a period of 2 years by the injection of dihydroergotamine, in 1-ml. dosage [? 1 in 1,000]. To obviate the need for injection, she was then given tablets containing 1 mg. of ergotamine and 100 mg. of caffeine. About half an hour after taking, for the first time, 2 of these tablets she became seriously ill, with vomiting, precordial pain, palpitations, cramps in the muscles, and numbness. She was cyanotic, with a barely palpable pulse and cold extremities. She recovered completely in about a day. Since then the administration of 0.5 ml. of dihydroergotamine or 1 mg. of ergotamine in a suppository has caused no trouble and has given prompt relief of the headache. The second patient was a woman of 41 with a history of migraine for 10 years. For about a year she gave herself injections of 1 ml. of dihydroergotamine one or more times a month, with complete relief. A period of increased nervous strain then began, the attacks of migraine became more frequent—twice or thrice weekly—and the injections were slower in their effect. She lost 30 lb. (13.6 kg.) in weight in 6 months from anorexia and vomiting. Her electrocardiogram (ECG) was normal. A fortnight later she took three injections within a week and, after the third, suffered from precordial pain which did not diminish under treatment. The ECG now showed signs of coronary disturbance which per-



sisted for 2 months. Recovery was incomplete after several months. This is believed to be the first reported case of toxic effects from dihydroergotamine, and malnutrition is considered to have contributed to their occurrence. The authors think that this, and hypertension even in the absence of vascular or renal lesions, should be added to the list of contraindications to the use of ergot derivatives in treating migraine.

Reginald St. A. Heathcote

## INDUSTRIAL TOXICOLOGY

### 84. The Successful Treatment of Two Recent Cases of Cyanide Poisoning

A. L. POTTER. *British Journal of Industrial Medicine* [Brit. J. industr. Med.] 7, 125-130, July, 1950. 15 refs.

Poisoning with cyanide salts is usually the result of accidental ingestion, whereas with hydrogen cyanide itself the risk is that of inhalation, but in certain circumstances either can be absorbed through the skin. Cyanides readily combine with methaemoglobin, and substances which promote methaemoglobin formation have therefore been used experimentally as antidotes in cyanide poisoning, though many of them are themselves toxic. The best results have been obtained in such experiments with the intravenous injection of sodium nitrite followed by sodium thiosulphate. The former assists in the formation of cyanmethaemoglobin, which is relatively non-toxic, from methaemoglobin, and the latter accelerates the conversion of cyanide to thiocyanate which is the normal process of detoxication and excretion. Up to 1944, in 14 out of 15 cases of cyanide poisoning in man treated by this means the patient recovered.

In a group of British factories manufacturing hydrocyanic acid and cyanides, emergency kits have long been provided, containing solutions of nitrite and thiosulphate ready made up in ampoules, sterile syringes, amyl nitrite capsules, and instructions to first-aid workers and doctors (which are reproduced in full). Treatment is started by the administration of oxygen and carbon dioxide and of amyl nitrite by inhalation while the syringes are being filled, artificial respiration being employed if necessary. Then a dose of 0.3 g. of sodium nitrite in 10 ml. of sterile distilled water (for a patient of 60 kg.) is slowly injected intravenously, followed immediately by 25 g. of sodium thiosulphate in 50% solution in sterile water. The stomach is washed out if necessary, and the patient is kept under observation for 24 to 48 hours, during which time these doses may have to be repeated. In 2 recent cases of accidental poisoning (described in detail) the method was successfully used. In one case cyanide intoxication was presumed, since the liquid acid had run over the man's bare hand; in the other case cyanide was detected in the blood. Both victims, chemical process workers, were suddenly taken ill and rapidly became unconscious, but after treatment were able to return to work some days later. The effect of treatment is dramatic, but success depends on the immediate availability of the nitrite and thiosulphate solutions. [Full details are given of the instructions included in the emergency kits.]

J. N. Agate

### 85. Psychical Disturbances in Chronic Mercury Poisoning. (Contribution à l'étude des troubles psychiques du mercurialisme chronique)

M. GOUSENBERG. *Monatsschrift für Psychiatrie und Neurologie* [Mschr. Psychiat. Neurol.] 120, 38-102, July, 1950. Bibliography.

It is pointed out that the effects of mercury on the young, as observed by Feer in those susceptible to calomel, do not resemble those noted in adults. In children there may be obvious allergy to the metal which lessens or disappears in later life. Some errors have arisen in industrial poisoning because the effects of other toxic substances, also present in a factory, have been overlooked. Among such are nitrous fumes, often found in explosives factories. A useful measure of the possibility of mercury poisoning may be gained by estimating the loss of metallic mercury in a given process; in some works several tons are unaccounted for each year, so that the employees are clearly exposed to considerable hazard. Stock noted the amount of mercury excreted by 9 workers; the urinary excretion varied from 600 to 17  $\mu$ g. per litre. The amount recovered in water used for washing the hands is also a useful index of the degree of exposure. In many employees the excretion greatly exceeds normal figures, yet there are no symptoms of poisoning, suggesting some acquired tolerance to the metal.

The psychic changes noted in mercurialism have been briefly described as an anxiety state with a tendency to panic. Hurried and uncertain movements betray a feeling of insecurity. Blushing and pallor are noted, with an expression of confusion. There is lability of mood with flight of ideas, and tremor increases when the subject thinks that he is observed. Movements needing some dexterity are difficult. Lassitude, insomnia, nightmare, and hallucinations may occur. In addition to symptoms presumably of organic origin, apathy and discouragement are not uncommon. Fits of temper, immediately regretted, may develop, but there may be timidity and hesitation. Loss of libido may have serious marital consequences. Rorschach's test has been used to demonstrate affective changes. Intelligence is somewhat diminished, memory weakened, and attention poor.

The author examined 11 patients, all of whom were making insurance claims. It appeared probable that many of the symptoms described were hysterical or due to a desire to substantiate a claim for compensation. Some of the patients complained of fatigue and exhaustion, yet were able to perform fairly heavy work or to move briskly after leaving the clinic. Others complained of headache and the early onset of fatigue after intellectual effort. Loss of concentration, depression, and irritability were frequent.

Preventive measures may be difficult to apply. An experienced workman may resent and try to avoid transfer to a task in which exposure to mercury is less or absent. The factory doctor should watch for mercurial tremor, nervousness, intolerance of alcohol, or loss of libido. A handwriting test performed after muscular effort is a valuable guide to the degree of incoordination present. After recovery from an attack of mercurialism

a subject is more sensitive to the metal than before. Delayed poisoning may also occur. Many employees, clearly affected by the poison, may cheerfully continue at work with insight into their condition, knowing that they are receiving higher pay because of the danger involved. Those of poor intelligence but aware of their disabilities may exaggerate their symptoms and develop a persecution state. In reviewing the literature the author was struck by the great diversity of signs and symptoms; no clear-cut syndrome can really be described.

It is necessary in all cases to take into account the individual peculiarities of the patient, notably in the psychiatric sense, for this will determine to a great degree the symptoms developing in mercurialism.

G. C. Pether

#### 86. The Toxicity of Methyl Iodide: I. Preliminary Survey

M. BUCKELL. *British Journal of Industrial Medicine* [Brit. J. industr. Med.] 7, 122-124, July, 1950. 7 refs.

The investigation described into the toxicity of methyl iodide arose from a proposal to use methyl iodide in fire extinguishers. Inhalation experiments were carried out on mice exposed to various atmospheric concentrations of methyl iodide in a chamber from which air samples for analysis were taken, the iodide being trapped in alcoholic potash (KOH) at  $-5^{\circ}\text{C}$ . and estimated as iodine after hydrolysis. Short exposures to concentrations of from 5 to 85 mg. per litre always caused death within 24 hours. A concentration of 1 mg. per litre caused death after repeated daily exposures totalling 11 to 43 hours, but repeated exposure to 0.5 mg. per litre was not lethal. The 50% lethal exposure time at 5 mg. per litre was 57 minutes. By subcutaneous or oral administration the approximate lethal dose for rats (determined by Deichmann's method) was 0.15 to 0.22 mg. per kg. body weight. Methyl iodide applied to human skin and covered up causes erythema, followed some hours later by vesiculation. Some evidence is given for considering methyl iodide at least as toxic as methyl bromide, and about ten times more toxic than carbon tetrachloride. There is likely to be a time-lag between exposure and the onset of symptoms, and clothing contaminated with methyl iodide must be removed at once.

J. N. Agate

#### 87. Absorption and Elimination of Inhaled Benzene in Man

J. SRBOVÁ, J. TEISINGER, and S. SKRAMOVSKY. *Archives of Industrial Hygiene and Occupational Medicine* [Arch. industr. Hyg. occup. Med.] 2, 1-8, July, 1950. 2 figs., 10 refs.

An account is given of 27 experiments carried out at Charles University, Prague, on 23 volunteers, who inhaled mixtures of benzene vapour and air, the concentration of benzene ranging from 150 to 350  $\mu\text{g}$ . per litre. After periods of inhalation of 2 to 3 hours the benzene content of the subject's blood, urine, and exhaled air was estimated polarographically until the values were no longer significant. It was found that different subjects retained amounts of benzene varying between 33 mg. and 198 mg. during 2 hours' inhalation;

the reason for variation in absorptive capacity is discussed. No subjective symptoms resulted. A considerable part of the absorbed benzene was excreted by the lungs (16.5% in 6½ hours), and a much smaller quantity by the kidneys (0.05% in 12 hours), the remainder being retained and metabolized. Equations are given by which the time necessary for inhaled benzene to be eliminated from the body may be calculated.

L. W. Hale

#### 88. Pulmonary Manifestations of Gasoline Intoxication. A Review with Report of a Case

R. ZUCKER, E. D. KILBOURNE, and J. B. EVANS. *Archives of Industrial Hygiene and Occupational Medicine* [Arch. industr. Hyg. occup. Med.] 2, 17-24, July, 1950. 3 figs., 20 refs.

Commercial gasoline [benzine, petroleum spirit] is a mixture of volatile hydrocarbons and may cause irritative lesions of the skin, conjunctiva, or pharynx. It may be absorbed via the pulmonary or gastro-intestinal system, and may cause disturbances of the central nervous system. Pneumonia, bloody pleural effusion, emphysema, and lung abscess have been described as occurring after aspiration of gasoline. The literature is briefly reviewed and the case is described of a man who inhaled gasoline when attempting to siphon it from a car tank. He developed bilateral pneumonia, predominantly right-sided, with right pleural effusion, the onset being (as is usual) within 24 hours of inhalation. Recovery followed a period of critical pneumonic illness.

L. W. Hale

#### 89. Acute Toxicity of Inhaled Beryllium. III. Observations Correlating Toxicity with the Physicochemical Properties of Beryllium Oxide Dust

R. H. HALL, J. K. SCOTT, S. LASKIN, C. A. STROUD, and H. E. STOKINGER. *Archives of Industrial Hygiene and Occupational Medicine* [Arch. industr. Hyg. occup. Med.] 2, 25-48, July, 1950. 8 figs., 23 refs.

An account is given of the effects on experimental animals of inhalation of air containing beryllium oxide dust in various grades and concentrations for periods of 6 hours, 5 days a week, the total exposure ranging from 56 to 360 hours. No pathological changes were found post mortem, save in the lungs. Tissue analysis showed by far the greatest amounts of beryllium in the lungs and pulmonary lymph nodes; small quantities occurred in liver, spleen, and bone.

The effects observed both before and after death varied with the grade of beryllium oxide inhaled, particularly with the particle-size and state of aggregation. Dyspnoea, anorexia, and loss of weight were observed in all animals exposed to high concentrations of beryllium. Death was accompanied by cyanosis. In view of the fact that human chronic pulmonary berylliosis produces cor pulmonale, haematological studies were made; polycythaemia was not noted, but a macrocytic hypoplastic or aplastic anaemia is described. Hyperglobulinaemia was noted, similar in degree to that in other chronic granulomatous diseases. Diffuse and focal pulmonary granulomatosis with fibrosis, as described in chronic

berylliosis in human subjects, were not found, the animals showing acute inflammatory bronchial and pulmonary changes.

L. W. Hale

**90. The Effect of Aluminium Dust on the Animal Organism.** (Действие алюминиевой пыли на организм животных)

M. G. IVANOVA and I. S. OSTROVSKAJA. Гигиена и Санитария [Gigiena] No. 4, 21-27, April, 1950. 2 figs.

The authors consider that insufficient study has been devoted to the value of aluminium inhalation in preventing silicosis. The experiments performed in Canada by Denny, Robson, and Irvin showed that quartz dust was absorbed more slowly from lung tissue if aluminium had previously been inhaled, but in the authors' view the period of observation was too short to permit of adequate conclusions; they suggest that commercial views have prevailed against scientific evidence.

They also think that a fundamental weakness in this method of prevention is the impossibility of gauging the amount of aluminium dust which should be used. Even if, theoretically, the addition of 1% of aluminium dust to the silica prevents or lessens absorption, there is no absolute proof that this is the ideal proportion. They do not agree that the introduction of aluminium dust into the body is essentially harmless, as some Canadian authors have suggested. According to Gardner aluminium has no retarding effect on silicosis, for the disease progresses despite its use. Lanza and Berry have noted that the introduction of aluminium into the blood stream or under the skin may have a toxic effect, paralyses developing in the central nervous system and the heart. In mammals tremor, loss of sensation, and progressive paralysis have been observed. Aluminium preparations are used as sclerosing agents, and this action is due to the formation of dense tissue round the particles and to changes in the tissue protein in contact with aluminium solutions.

Lung lesions are not uncommon in workers in aluminium factories, a matter worth consideration when the therapeutic use of the metal is contemplated.

The authors experimented on white rats and rabbits by: (1) intratracheal administration of aluminium powder in physiological saline (white rats only); (2) intravenous injection of the same solution (rabbits); (3) exposure to the dust in closed chambers (rats and rabbits). A very fine dust was used with particle size not exceeding  $2 \mu$ . For the intratracheal injections 0.01 g. of powder was suspended in 3 ml. of saline, of which suspension one-third was used.

The first experiments showed that the powder was far from harmless. In a rat killed 3 months after the intratracheal injection, nodules of fibrous tissue were found, mostly in the terminal bronchioles. Some of this tissue showed hyaline change with obliteration of vessels. Attempts were made to determine the first pathological changes and the sequence of changes. In particular the fate of the dust particles, and the possible phagocytosis of these, were of interest. It was hoped to discover why fibrotic changes occurred, and also the general systemic effect of any aluminium which might be absorbed into the circulation.

The second series of rats was exposed to aluminium dust averaging 5,000 particles per c.cm. for half an hour every day. Some were allowed to die naturally and others were killed at intervals. Others were exposed to dust for 8 hours daily for 15 days. At necropsy many cells in the alveoli and adjacent tissues were filled with dust, so that the nuclei were often indistinguishable. There was marked local leucocytosis with obliteration of some of the finer air spaces. Rats killed after 2 or 3 months showed, in addition to the changes described, marked peribronchial fibrosis with perivascular thickening and narrowing of the lumen.

In all animals studied the dust was evidently taken up by the alveolar epithelium and carried into the adjacent tissues, but the regional lymph nodes were almost free of dust because of blocking of the intercommunicating lymphatics. Sclerosis continues even when exposure to dust has ceased. Similar results were noted in rabbits. It is evident that the changes represent a severe aluminosis with, in some cases, superadded pneumonic changes and death. Pathological changes were seen in the kidneys and sometimes in the heart and other organs. It is concluded that the prophylactic use of aluminium needs further study, as also the lungs of the workers handling this metal.

G. C. Pether

## THERAPEUTICS

**91. Bone-marrow Infusions: Intratibial and Intravenous Routes Compared**

L. W. C. MASSEY. *British Medical Journal* [Brit. med. J.] 2, 197-198, July 22, 1950. 25 refs.

In the treatment of infants with gastro-enteritis 72 intratibial and 72 intravenous infusions were successfully performed. The intratibial infusions were given by Gimson's method, and the intravenous infusions were given usually into the saphenous vein at the ankle, a double needle of the Bateman type being tied in. After intratibial infusion a mild periostitis was seen in all cases examined radiologically (although only one case of frank osteomyelitis requiring surgical treatment occurred) while mild infection of the puncture wound was not uncommon. On the other hand, after intravenous infusion some degree of phlebitis was usual and 6 cases of manifest thrombophlebitis were noted. To sum up, the author considers that the advantages of the intratibial method are the ease and speed of introduction of the needle and its firm fixation, while the intravenous route not only permits a faster rate of flow, but is preferable when blood and plasma are given.

John F. Loutit

**92. Metabolic and Cardiovascular Studies of Prolonged Intravenous Administration of Human Serum Albumin**

N. S. GIMBEL, C. RIEGEL, and W. W. W. L. GLENN. *Journal of Clinical Investigation* [J. clin. Invest.] 29, 998-1009, Aug., 1950. 4 figs., 29 refs.

An experiment was undertaken with the object of ascertaining the fate of human serum albumin when given by infusion for a prolonged period. Three healthy young



volunteers were given daily doses of albumin (supplemented with 4% DL-acetyltryptophan) varying from 30 g. to 75 g. both orally and intravenously for periods of 6 to 17 days, during which they took a basic diet containing less than 0.5 g. of nitrogen daily. Before, during, and after each period comprehensive studies were made of nitrogen balance, protein content of blood plasma, interstitial fluid, lymph, and cerebrospinal fluid, potassium balance, urinary sulphate excretion, plasma volume, and the state of the cardiovascular system.

During the intravenous infusion periods large amounts of albumin accumulated in the plasma, the interstitial fluid, and the lymph, and albumin catabolism increased until nitrogen equilibrium was attained. When the albumin was given by mouth this equilibrium was achieved only with the administration of not less than 75 g. There was some indication that part of the infused albumin was used for the formation of cellular protoplasm. In some of the experiments severe congestive heart failure developed in these healthy young males when 50 g. of albumin had been given intravenously daily for a week. Albuminuria commonly developed. It is concluded that cardiovascular complications due to overloading of the circulation are a real danger and may seriously limit the usefulness of intravenous human albumin as a nutritional supplement except in those cases in which there is actual deficit of serum albumin.

A. I. Suchett-Kaye

#### 93. Hypocoagulability of Certain Irradiated Plasmas

S. S. CUTLER, B. BURBANK, and E. R. MARZULLO. *Journal of the American Medical Association [J. Amer. med. Ass.]* **143**, 1057-1059, July 22, 1950. 4 refs.

Human plasma used for transfusion is now often irradiated with ultraviolet light to inactivate the virus of homologous serum jaundice. Whereas certain samples of irradiated plasma, either liquid or dried, were clotted rapidly by a standard amount of thrombin, the liquid irradiated plasma from another source was not clotted even by one hundred times that amount of thrombin. Experiments are quoted to show why some of this effect may be due to heparin-like substances.

It is suggested that the cause of the difference between the two products may lie in the quality of the radiation. The affected plasma had been irradiated by ultraviolet light with a high component in the Schumann region (1,751 to 2,026 Å). The unaffected plasma, on the other hand, was irradiated by light in which 0.1% of the energy fell in this region.

John F. Loutit

#### 94. The Plasma Substitute, Dextran, and Blood Pressure Regulation. (Le dextran, succédané du plasma sanguin, et homéostasie de la pression artérielle)

G. VAN DEN HEUVEL-HEYMANS. *Archives Internationales de Pharmacodynamie et de Thérapie [Arch. int. Pharmacodyn.]* **83**, 308-318, 1950. 3 figs., 32 refs.

It is shown that, after massive haemorrhage in dogs, the intravenous infusion of an equal volume of 6% solution of "dextran" can restore to normal the blood pressure and respiration, and also the pressor response to carotid-artery occlusion. This is equally true if the re-infusion is started 5 minutes or 90 minutes after the

end of the bleeding. In some animals there is a secondary fall in blood pressure after 3 or 4 hours, as the smallest molecules in the dextran solution are eliminated. In many animals, however, the blood pressure and pressor reflex remain normal for at least 7 to 8 hours without further infusion.

Derek R. Wood

#### 95. Haemolytic Transfusion Reaction due to Anti-M Sensitization. (Réaction transfusionnelle hémolytique due à une sensibilisation anti-M)

A. S. WIENER. *Revue d'Hématologie [Rev. Hémat.]* **5**, 3-6, 1950. 5 refs.

#### 96. Infra-red Heating of Tissues

F. X. SWEENEY, S. M. HORVATH, H. C. MELLETTE, and B. K. HUTT. *Archives of Physical Medicine [Arch. phys. Med.]* **31**, 493-501, Aug., 1950. 5 figs., 7 refs.

The effectiveness of near and far infra-red irradiation in heating the deep tissues has been a very controversial point. Comparing the effects of five different infra-red lamps under field conditions, the authors came to the conclusion that for conventional therapy neither type of source had any marked advantage. They noticed, however, that the far infra-red rays were able to penetrate the tissues directly, whereas the near infra-red sources penetrated the tissues by means of conduction and circulatory distribution.

M. H. L. Desmarais

#### 97. Local Effects of Microwave Radiation on Tissues in the Albino Rat

L. ESSMAN and C. S. WISE. *Archives of Physical Medicine [Arch. phys. Med.]* **31**, 502-507, Aug., 1950. 4 figs., 3 refs.

The authors describe the local tissue changes caused by thermal injury due to microwave irradiation of albino rats under standard experimental conditions and compare them with changes produced by infra-red radiation. They could not produce any gross or microscopic evidence of thermal injury to the deep tissues without causing superficial thermal burns. Where thermal injury was produced by microwave irradiation the tissue injury, macroscopic and microscopic, was deeper and more extensive in relation to the superficial lesion than that in similar animals injured by infra-red irradiation. They could find no difference as regards the threshold beyond which burns were produced between microwave diathermy and infra-red irradiation.

From their experiments they came to the conclusion that microwave radiation penetrates more deeply into the tissues than infra-red rays, but as the thermal threshold of the skin is the same for both, the skin sensation of heat is an adequate safeguard against thermal injury to the deeper tissues.

M. H. L. Desmarais

#### 98. Neuromuscular Re-education in the Rehabilitation of Cerebral Palsy

R. CAILLIET. *Occupational Therapy and Rehabilitation [Occup. Therap.]* **29**, 205-214, Aug., 1950. 20 refs.

## Medical Jurisprudence

99. **Rubella in Pregnancy: the Obstetrician's Problem**  
W. M. LEMMON. *Medical Journal of Australia* [Med. J. Aust.] 2, 392-394, Sept. 9, 1950. 9 refs.

The incidence of severe developmental defects after rubella in pregnancy has been over-estimated in earlier work. There is a probable chance of severe affection of the foetus in 25 to 50% of cases if the disease develops in the first 100 days of pregnancy.

The legal position for termination of such pregnancies is extremely difficult, the maternal life and health being in no danger, except that the worry of producing and looking after a handicapped child may cause mental strain. There is a place for termination in occasional cases after careful obstetrical and psychiatric consideration.

D. B. Fraser

100. **Positive Demonstration of Paternity.** (Der positive Vaterschaftsnachweis)  
M. LÖNS. *Zeitschrift für Hygiene und Infektionskrankheiten* [Z. Hyg. InfektKr.] 131, 371-385, 1950.

If it be assumed that the genetic constitution of each person is unique and derived by inheritance from the parents, so that all characters present in the child are present in one or other parent, then it ought to be possible to devise a method of determining definitely who is the father of the child of a particular woman rather than being satisfied, as at present, with the exclusion of some of the suspects. The author suggests that this might be done by immunizing animals with the erythrocytes of a very large number of different persons. If this polyvalent serum were added to the erythrocytes of the mother and the real father, all agglutinins for the child's erythrocytes would be removed, whereas if the erythrocytes of some man other than the real father were used for absorption, some agglutinins for the child's erythrocytes would remain. Tests of the method, with suitable controls and variations [for details of which the original paper should be consulted], suggested that it might be of value.

[It never seems to strike the author that the best test of the accuracy of his method would be to apply it to the erythrocytes of children whose parentage is not disputed, rather than to those of children of doubtful parentage. The paper is rather long, and, possibly owing to abbreviation of the tables, not very clear.]

C. L. Oakley

101. **Reflections on Criminal Conduct and its Treatment**  
D. K. HENDERSON. *British Medical Journal* [Brit. med. J.] 2, 311-315, Aug. 5, 1950.

In this paper, which is a memorandum submitted to the Royal Commission on Capital Punishment, the author states his belief that the violent methods of punishment and retribution which have received such universal approval in legal and public circles have little or no constructive value and make no contribution towards

social reformation. He pleads for an approximation of the legal view of insanity to that of the psychiatrist. The large army of recidivists is itself an indictment of the arbitrary sentence methods at present in vogue. A plea of mental disorder is advanced too often in serious cases and not frequently enough in trivial charges. At the time they were formulated, the McNaghten rules constituted a definite advance in legal thought and practice and were in conformity with current medical knowledge. Now they are no longer in harmony with medical knowledge and there are wide differences in their interpretation.

In the author's opinion it is quite impossible to define degrees of unsoundness of mind, and many different forms of mental disorder should equally excuse criminal conduct. Persons who are proved to be insane in a medical sense are, in the author's opinion, not legally responsible for the crime which they may commit. It is suggested that when the issue is a capital one there should be no rigid rules. The issue should be left for the judge to place before the jury and each case should be dealt with on its individual merits. The McNaghten rules are considered too rigid a yardstick when a life is at stake.

The law refuses to allow mental deficiency to be put forward as a defence in bar of trial or sentence except in the most gross cases. The author considers it a complete travesty to suggest that persons who can be certified as mentally defective should be allowed to plead to the charge against them, or be considered capable of instructing their defence and of being able to follow the evidence submitted to the court. He contends that mental deficiency of whatsoever degree should be regarded as an adequate defence in bar of trial or sentence, and that mentally defective persons who have committed criminal acts should be cared for under hospital or colony conditions. Individuals with psychopathic personalities constitute the most difficult problem. They are social misfits; they are not certifiable, but they constitute the greatest potential danger. They are not sane enough to be at large, and not insane enough to be forcibly confined in an institution. These were the cases responsible for the introduction of the doctrine of limited or modified responsibility which has been generally accepted in the Scottish courts. Criminals in this category should be cared for in special institutions similar to that at Herstedvester in Denmark, where there is a specially trained staff of psychiatrists, nurses, teachers, sociologists, and warders. The author advances a plea for a closer liaison between legal and medical practitioners, in order that each may learn to appreciate the point of view of the other.

Gilbert Forbes

102. **Traffic and Alcohol**  
P. H. ANDRESEN. *Medico-Legal Journal* [Med.-leg. J.] 18, 98-105, 1950. 2 figs.

# Radiology

## RADIOTHERAPY

### 103. The Experimental Application of Radioactive Colloidal Gold in the Treatment of Pelvic Cancer

A. I. SHERMAN, J. F. NOLAN, and W. M. ALLEN. *American Journal of Roentgenology and Radium Therapy* [Amer. J. Roentgenol.] **64**, 75-85, July, 1950. 14 figs., 21 refs.

The possibilities of treatment of uterine carcinoma, both by surgery and by irradiation, are limited by the anatomical conditions relating to the spread of the disease and by the difficulty encountered when the parametrium and regional lymph nodes are involved. The authors therefore set out to investigate the therapeutic potentialities of radioactive gold in this condition. The investigation was carried out in four stages. In the first series of experiments squamous-cell carcinoma in mice was treated by direct injection of radioactive gold ( $^{198}\text{Au}$ ) in colloidal form.  $^{198}\text{Au}$  has a half-life of 2.7 days and emits a beta radiation of 0.8 meV and gamma radiation of 0.44 and 0.28 meV. A particulate gold sol in gelatin was suspended in a 1% solution of pectin in 5% aqueous dextrose. Doses were measured by means of a Geiger-type counter and expressed as mc. per c.cm. of tumour tissue. Control experiments showed that the best results were obtained with doses of 200 to 300 mc. per c.cm., and animals receiving a total of more than 2 mc. died. With tumours 1 c.cm. or less in volume the cure rate was 100%. With larger tumours the cure rate fell in proportion to the size of the tumour.

The second series of experiments was designed to demonstrate the effects of the injection of  $^{198}\text{Au}$  into the parametrium of rabbits. Injections were made under direct vision through an abdominal incision with doses ranging from 1 to 25 mc. into various volumes of parametrial tissue. Biopsies from lymph nodes and other tissues were taken 72 hours after injection and again at 1, 6, and 12 weeks, and the specimens assayed for radioactivity and studied microscopically. Initially, the lymphatic vessels became filled with phagocytic cells of the mononuclear, polymorphonuclear, lymphocytic, and giant-cell types, containing gold particles in their cytoplasm. The lymph follicles draining the lymphatic vessels became filled with these scavenger cells, and cellular destruction accompanied the absorption of gold particles, being marked a week after injection. By this time the iliac lymph nodes were also involved, and showed radiation damage. Three months after the injection all affected tissues showed fibrosis and atrophy.

In the third set of experiments the effects of the intra-uterine application of radioactive gold on the proliferative response of the endometrium of the rabbit to ovarian hormones was studied. The introduction of a radioactive fluid into the uterine cavity would appear to be the ideal method of obtaining uniform dosage. It was

found that the progestational response of the endometrium to chorionic gonadotrophin was completely inhibited, the adjacent ovary also suffering radiation damage. The regional lymphatics and lymph nodes became infiltrated with gold, and were similarly affected. The final experiments were directed to the determination of tolerance levels of normal parametrial tissue in the rabbit. The dose of  $^{198}\text{Au}$  that could safely be administered, when expressed as concentration of radioactivity per c.cm. of parametrial tissue, was found to be between 1.25 and 1.75 mc., and was thus within the therapeutic range. The results of these experiments suggest that radioactive gold may be of use in the treatment of uterine carcinoma.

A. G. C. Taylor

### 104. Production of Malignant Tumors in Rats with Radioactive Phosphorus

S. KOLETSKY, F. J. BONTE, and H. L. FRIEDEL. *Cancer Research* [Cancer Res.] **10**, 129-138, March, 1950. 16 figs., 8 refs.

In experiments performed at the Western Reserve University School of Medicine, Cleveland, Ohio, adult male rats of the Wistar strain, in which spontaneous bone tumours have not previously been observed, were given single or repeated doses of radioactive phosphorus ( $^{32}\text{P}$ ) for the purpose of studying the process of repair in radiation injuries of various tissues and similar phenomena. The first group of rats received one intraperitoneal injection of 4.5  $\mu\text{c.}$  of  $^{32}\text{P}$  per gramme of body weight. Nineteen animals died or were killed between 6 and 12 months after the injection and complete necropsies were performed. Malignant neoplasms were detected in 9 of these, the interval since injection ranging from 210 to 360 days. In 6 cases the tumour was classified as an osteogenic sarcoma, 3 being of the maxillary bones, one of the tibia, one of the ilium, and one of a cervical vertebra. Metastases in the lungs were found in connexion with three of these tumours. In the remaining 3 cases the tumour was a squamous-cell carcinoma involving the face and associated with exophthalmos, and in one case metastases in the cervical lymph nodes were observed. The rats in the second group received, at intervals of 3 weeks, intraperitoneal injections of 1.5  $\mu\text{c.}$  of  $^{32}\text{P}$  per g. of body weight, up to a total of 8 injections in the 8 which survived, the others dying after 1 to 7 doses. In 4 rats malignant tumours were present 120 to 200 days after the first injection, the tumour in all 4 being classified as an osteogenic sarcoma and the site being the maxillary bone, the tibia with metastases to the lungs, the femur, and a lumbar vertebra respectively. All the sarcomata originated either in the metaphysis or the periosteum and consisted of highly pleomorphic or spindle-shaped cells and giant cells, with an abundant intercellular matrix. In almost all other rats atypical proliferation of bone was found in the femur and in the vertebrae.



The authors suggest that although the doses they employed were proportionately much larger than those used clinically, the therapeutic administration of large doses of any radioactive isotope which accumulates in the bones should be avoided.

L. Dmochowski

#### 105. Studies on Lymphocytes from Persons Treated with Radioactive Iodine

W. E. WATTS and D. R. MATHIESON. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] 35, 885-889, June, 1950. 4 refs.

With phase-contrast microscopy or supravital staining 34% of normal human lymphocytes are found to contain 1 to 8 refractile cytoplasmic granules. Striking increases in the number and frequency of these granules have been reported in the lymphocytes of persons exposed to ionizing radiations. The authors examined the blood of 2 patients with thyroid cancer and 8 with exophthalmic goitre who were being treated with radioactive iodine ( $^{131}\text{I}$ ), of 3 x-ray technicians with long exposure, and of 4 patients receiving massive x-ray treatment for malignant disease. No significant changes in the lymphocyte granules were found.

M. C. G. Israëls

#### 106. Radiation Therapy of Cancer of the Larynx

B. V. A. LOW-BEER. *Laryngoscope* [Laryngoscope, St Louis] 60, 696-717, July, 1950. 2 figs., 25 refs.

Since 1931, 219 patients with carcinoma of the larynx have been treated in the Division of Radiology of the University of California School of Medicine. Of these, 157 patients received a full course of x rays. The calculated tumour dose in the first 5 years was not more than 4,000 r; in the second 5 years it varied between 4,000 r and 6,000 r; and from 1941 to 1945 it ranged between 5,500 r and 7,500 r. The time of treatment varied between 28 and 35 days.

In 16 patients treated with neutrons generated in the cyclotron the reaction was more severe than in those treated with x rays. In 7 of these patients necropsy showed no cancer cells in the treated areas, but in all there were deep necrotic ulcers. In advanced cases perichondritis is likely, and antibiotics should be given during treatment. In the first 5 years 1 patient in 10 with intrinsic cancer survived for more than 5 years, in the second 5 years 6 out of 16, and in the third 5 years 21 out of 47 survived for the same period. Between 1936 and 1945, of 20 patients with extrinsic carcinoma, only one patient survived for longer than 5 years. The use of several fields means that some areas receive more radiation than others, but the use of a single field should be confined to the treatment of small tumours.

William McKenzie

#### 107. X-ray Treatment for Peptic Ulcer Does not Appear to Damage the Heart

N. E. GOULDER, W. J. CARPENDER, and E. LEVIN. *Gastroenterology* [Gastroenterology] 15, 264-270, June, 1950. 2 figs., 12 refs.

Twelve patients treated for duodenal ulcer by x-irradiation of the gastric fundus were studied for 6 weeks after the conclusion of treatment. Clinical, electro-

cardiographic, and radiological observations were made and from these it was concluded that such treatment involves no risk of cardiac injury. Minor, transient changes in the ventricular complex of the electrocardiograms were not thought to be of any significance.

John Naish

#### 108. Sudeck's Syndrome and its Cure by X-ray Therapy. (Über das Sudecksche Syndrom und seine röntgentherapeutische Heilung)

H. MEYER-LAACK. *Strahlentherapie* [Strahlentherapie] 82, 231-246, 1950. 5 figs., 6 refs.

A brief clinical and histological account of Sudeck's syndrome is given; the atrophy affects not only bones, but also the neighbouring soft tissues and skin. The vascular changes are not ascribed, as is usually the case, to a local effect on the peripheral sympathetic nervous system, but to a wider reflex functional disturbance of the sympathetic. The most extreme form is seen in causalgia. Difficult cases may need 2 to 3 years of conventional treatment.

Three cases are described in which x-ray therapy gave excellent results in 2 to 3 months. The technique was adjusted to each case, deep x rays being used at 180 kV, with focus-skin distance 40 cm. and a filter of 0.3 mm. Cu. In the first case, involving the wrist, radiation was applied to: (1) the wrist area with a 10×8-cm. field and dose of 150 r; (2) the axilla, to irradiate the sympathetic perivascular fibres, with a 8×10-cm. field and dose of 120 r; (3) the cervical region, to irradiate the sympathetic ganglia (8×10-cm. field, 120-r dose). Doses were given three or four times at intervals of 4 to 6 days. After a striking initial success, the wrist field was given a second series of four doses of 200 r each 3 months later. In the second case, involving the knee, a 20×24-cm. field was used, including the knee and the peripheral sympathetic system: 150 r was given from each side at 120 kV on three occasions at 5-day intervals; after 4 weeks a second course was given, with a 150-r dose from each side alternately, for four doses; irradiation of additional fields was not necessary. In the third case, involving the radius, only the neck was irradiated, through an 8×10-cm. field from each side; the dose of 150 r was repeated four times at 4-day intervals. Six weeks later two further doses of 150 r were given; no further irradiation was needed.

J. Walter

#### 109. Treatment of Simple Epithelial Cysts with Secondary Photoelectron Radiation. Preliminary Report

L. COHEN and S. A. KIMMEL. *British Medical Journal* [Brit. med. J.] 2, 87-88, July 8, 1950. 1 fig.

The occurrence of "plunging ranula" (a cystic swelling originating in the floor of the mouth and extending into the neck) was found to be not uncommon in children attending the Non-European Hospital, Johannesburg, and its treatment by surgery or sclerosing injections proved unsatisfactory, while conventional x-ray therapy with moderate doses was completely ineffective. It is well known that the presence in irradiated tissue of an element of high atomic number greatly increases

the secondary photo-electric emission, and the authors therefore investigated the possibility of introducing a heavy element in solution into the cyst and destroying the secretory lining by the intense local ionization produced by its irradiation with medium-voltage x rays.

The technique adopted was to aspirate the ranula contents through a wide-bore needle under local analgesia and to introduce into the cavity 2 ml. of a 10% aqueous solution of bismuth oxychloride ("bisoxyl"). This was followed by exposure to x rays at 140 to 180 kV, delivering about 300 r to the tissue at a single sitting. Reactions noted were a brisk effusion into the cyst, lasting a week, followed by steady shrinkage of the mass, which in 3 weeks became a small fibrous nodule.

Detailed accounts are given of 4 cases, showing the effect of bismuth injection alone and the greater efficacy of the combined injection-irradiation method. After one year's experience of this procedure, the authors have encountered no failures and no recurrences.

[The effective dose of ionization at the cyst wall is difficult to estimate, depending as it does on the distribution of the suspended bismuth in the cyst fluid. The work of Spiers (*Brit. J. Radiol.*, 1946, **19**, 52) is of interest in this connexion.]

Arthur Jones

#### 110. Treatment of Hodgkin's Disease with Roentgen Irradiation and Nitrogen Mustards

F. H. BETHELL, G. A. ANDREWS, R. B. NELIGH, and M. C. MEYERS. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 61-74, July, 1950. 8 figs., 17 refs.

The authors review a series of 173 cases of Hodgkin's disease treated at the University of Michigan Hospital during the 10-year period beginning July 1, 1938, the follow-up being complete up to the beginning of 1948. In all cases the diagnosis was confirmed histologically at some stage of the disease. Irradiation was used in the treatment of 138 patients in the series, and 5 received nitrogen mustard in addition. The 5-year survival of 119 cases treated by irradiation was found to be 19.3%, and the 10-year survival about 10%. Among the manifestations of the disease the authors list fever, pruritus, intrathoracic complications, splenomegaly, anaemia, abnormalities in the leucocyte count, and a raised erythrocyte sedimentation rate. It is claimed that the presenting feature may be significant as an index to future progress, splenomegaly and a leucocyte count above 10,000 or below 6,000 per c.mm. indicating a poor prognosis.

A preliminary survey is given of the results of treatment with nitrogen mustard of 30 patients, most of whom were in an advanced stage of the disease. The basic dose was 0.1 mg. per kg. body weight, with a maximum of 6 mg. Four injections were given intravenously on alternate days, and a minimum of 5 weeks was allowed to elapse before a further course was given. An important toxic effect of nitrogen mustard is depression of bone-marrow activity. A fall in the circulating haemoglobin level and erythrocyte count is common, but need not cause concern. A leucopenia occurs in about 60% of patients treated, the leucocyte count tending to fall progressively for 2 to 3 weeks, returning to normal in a further 5 to 6 weeks. Infection secondary to the leucopenia can

usually be avoided by the judicious use of antibiotics. Clinical remissions induced by nitrogen mustard varied in duration from a few days to several months, the longest interval between courses being 8 months. It was found to be of most use in advanced cases previously treated by irradiation; 9 out of 16 cases in this category, when treated with nitrogen mustard alone or supplemented by irradiation, were controlled for a minimum period of 6 months. Another group who appeared to benefit from nitrogen-mustard therapy were those patients with moderately advanced disease and post-irradiation tissue damage, the disease being controlled for a minimum period of 6 months on nitrogen mustard alone in all 4 patients in this category.

The choice of therapy in Hodgkin's disease must be governed by the extent and stage of the disease. When the process appears to be localized to one area, surgical excision of the affected nodes followed by irradiation may eradicate the disease, but for most patients suppression of activity is the most that can be achieved. This may be effected by irradiation alone in early cases, and by irradiation combined with nitrogen-mustard therapy in the more advanced cases. The nitrogen mustards have so far proved of greatest value (1) as a supplement to irradiation in cases of moderately advanced disease which is still responding to irradiation, with a view to minimizing radiation damage to healthy tissues; (2) in cases with extensive visceral, particularly abdominal, involvement; (3) in cases of chronic, progressive disease in which irradiation has been used to the limits of safety. The contraindications to the use of nitrogen mustard are few, but it should be used with caution, and it is doubtful whether it should ever be given where there is evidence of liver damage.

A. G. C. Taylor

### RADIODIAGNOSIS

#### 111. Experiences with the Use of Direct Aortography in the Diagnosis of Coarctation of the Aorta

W. H. MULLER and R. H. SLOAN. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **20**, 136-141, July, 1950. 5 figs., 5 refs.

The diagnosis of aortic coarctation is usually made with ease, but the exact site and extent of the narrowed segment can be determined only by radiography with contrast media. Intravenous injection of diodone produces too diffuse a picture of the aorta in many instances. Retrograde injection into the carotid gives better contrast, but is a more formidable procedure and not without risk. Crafoord's method of introducing a catheter into the ascending aorta via one or other radial artery gives an adequate picture of the coarctation, but relatively large amounts of diodone are required and there is a risk of occluding one of the coronary vessels.

The authors have modified this last method and attempt to place the catheter in the descending aorta just above the constriction; in this way, it is claimed, injection of a relatively small volume (25 ml.) of contrast medium will give good results. The catheter is passed along the left radial artery until it meets with obstruction, which usually occurs where the subclavian artery takes an

abrupt downward bend into the mediastinum. Its position is determined on the x-ray screen, the arm is abducted to 90 degrees, and the catheter passed further until it is lying just in the aortic lumen. The contrast medium is then injected and serial films are taken. The chief disadvantage of this method is that the ascending aorta and its branches are not visualized.

W. P. Cleland

#### 112. Horizontal Body Section Radiography

J. J. STEVENSON. *British Journal of Radiology* [Brit. J. Radiol.] 23, 319-334, June, 1950. 30 figs., 11 refs.

The apparatus employed at the Royal Cancer Hospital, London, first developed in 1937 and modified in 1939, for horizontal sectional radiography is described. It involves a special application of the widely used planigraphic principle.

The patient sits upright upon a revolving seat. Alongside is mounted a horizontal cassette tray, which is geared to, and can be rotated synchronously with, this seat. The x-ray tube is mounted in such a way as to project its central ray downwards through the patient to the film at an angle of about 30 degrees with the horizontal.

All body structures which lie in the plane corresponding with the point of intersection of the central ray and the axis of rotation of the subject retain their relative positions on the film and thus are rendered sharp on the radiograph. The plane is varied by raising or lowering the patient.

The method is suited to radiography of the thorax, and the author gives illustrations of the normal thoracic contents at different levels, following this by examples of the value of this technique in the diagnosis of abnormal conditions of the great vessels, retrosternal goitre, carcinoma of the bronchus, and pulmonary cavitation.

A. M. Rackow

#### 113. Psychiatric Surgery. Post-operative Control with Iodized Oil in Gelatin. (Psycho-chirurgie. Controle radiologique post-opératoire par la gélatine lipiodolée)

J. LE BEAU and J. PECKER. *Presse Médicale* [Pr. méd.] 58, 777-778, July 5, 1950. 7 figs., 5 refs.

Many different types and modifications of prefrontal leucotomy are in use at the present time; the necessary evaluation of these different methods depends, among other things, on the post-operative radiological determination of the exact site of the cut or cuts carried out. Several procedures may be used, such as the injection of iodized oil or the use of clips or silver wire, to make it possible to recognize on the x-ray film the site of the incision or resection. In the authors' opinion these methods are unsatisfactory. They recommend the use of thin pieces of gelatin sponge (as used for haemostasis), which are soaked in "lipiodol" for several minutes and then placed in the cerebral incision or upon the site of the cortical resection. This procedure is said to have the following advantages: (a) it helps to secure haemostasis; (b) x-ray films show very well the exact site of the incision; (c) gelatin sponge and lipiodol are completely absorbed within a month.

F. K. Kessel

#### 114. The Ventricles in Temporal Tumour. (Das Ventrikelbild der Temporalumoren)

R. LORENZ. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [Fortsch. Röntgenst.] 73, 199-212, June, 1950. 27 figs.

The aetiology and site of temporal tumours are varied. Meningiomas appear in the sphenoidal ridge, in the floor of the middle fossa, in the Sylvian fissure, in the temporal pole, in the Gasserian ganglion, and in the tuberculum sellae. Other tumours may also be present, such as glioblastomata, astrocytomata, oligodendrogliomata, abscesses, arterio-venous aneurysms, metastases, tuberculomata, subdural haematomata, dermoids, and teratomata. Lysholm divides tumours into those which cause no change in radiological appearance in the temporal lobe and those which do. Tumours of the Sylvian fissure cause no displacement of the temporal lobe. Medially situated tumours of central ganglia cause little change in the appearances of the temporal lobe.

From the radiological point of view, temporal tumours may be divided into: (1) lateral temporal tumours (anterior and posterior); (2) basal temporal tumours; (3) tumours of the Sylvian fissure; (4) medial temporal tumours. By ventriculography these can be easily differentiated. The author takes the following films as a routine: antero-posterior sagittal and lateral, postero-anterior sagittal and lateral, right and left lateral, and half-axial antero-posterior and postero-anterior. The two latter are of the greatest diagnostic value. When in these two films the temporal lobe is not filled, or when in the half-axial film with the patient supine the temporal lobe is shown to be compressed, the diagnosis of temporal tumour is justified. The farther the temporal tumour is from the temporal horn, the more difficult is the diagnosis.

The author describes 27 cases of temporal tumour, in 19 of which ventriculography was performed. The factors influencing the ventriculographic picture are described. Anterior temporal tumours deform the ventricles in a different way from Sylvian-fissure or posterior tumours. Anterior temporal tumours alter the appearances of the temporal horn very little, but the latter is displaced by tumours of the Sylvian fissure. Posterior temporal tumours almost completely obliterate the temporal horn, flatten it, and displace it medially. No temporal tumour influences the position of the anterior horns or of the third ventricle. The cella media runs obliquely from the front and from the sound side to the diseased side and posteriorly, and is sometimes displaced to such an extent that no air can be introduced into the diseased posterior horn, and an erroneous diagnosis of occipital tumour may be made. In 6 out of 19 cases the capacity of the ventricular system was normal, in 9 cases there was a moderate dilatation, and in 4 cases there was some dilatation on the sound side.

Lysholm stresses the importance of the sagittal film taken with the patient in the supine position. Displacement of the temporal horn helps to distinguish medial from lateral tumours. If, however, filling is insufficient, the temporal horn will not be shown at all. Sagittal films in the frontal position and half-axial ones



are then helpful. The cella media is displaced towards the sound side and the posterior horns appear normal. The author compares the appearance of the posterior part of the ventricle to a bird's wing, and claims that this appearance justifies the diagnosis of temporal tumour. Plain radiographs show whether the tumour is invading bone. Cerebral angiography may help in these cases, but its results are not always conclusive. A summary of the ventriculographic appearances in temporal tumour is given, together with an analysis of the differential diagnosis.

W. J. Czyzewski

#### 115. Acromioclavicular Changes in Primary and Secondary Hyperparathyroidism

L. NATHANSON and M. SLOBODKIN. *Radiology* [Radio-logy] 55, 30-35, July, 1950. 8 figs., 13 refs.

Acromioclavicular changes are described in 3 cases of hyperparathyroidism, both of the primary type and of the secondary type due to chronic renal insufficiency. Attention is directed to these changes in the hope that they will be checked and commented upon by other observers. The negative value of absence of these changes is stressed as an aid in the differential diagnosis of hyperparathyroidism.—[Authors' summary.]

#### 116. The Meniscus as a Radiological Sign of Infiltrating and Ulcerated Cancer of the Oesophagus. (Le ménisque, traduction radiologique des cancers infiltrés et ulcérés de l'œsophage)

A. GUÉRET, A. LAMBLING, M. CACHIN, and M. CONTE. *Archives des Maladies de l'Appareil Digestif* [Arch. Mal. Appar. dig.] 39, 653-660, June, 1950. 6 figs., 1 ref.

The radiological findings in 4 cases in which a carcinoma of the oesophagus showed as a meniscus are reported. The authors are interested in the idea that the malignant ulcer with its thick edge shows as a meniscus if the film is taken in true profile, but that the appearances may be difficult to interpret at any other angle. They consider that serial films should be taken of the oesophagus at slightly different angles if there is any question of a lesion being present.

Denys Jennings

#### 117. The Radiological Diagnosis of Bronchial Carcinoma as a Preliminary to Pneumonectomy. (Die Röntgendiagnostik des Bronchialkarzinomas als Voraussetzung zur Pneumonektomie)

A. LEB. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [Fortsch. Röntgenst.] 73, 141-150, June, 1950. 7 figs., 39 refs.

The author reports on 137 cases of bronchial carcinoma examined in the course of 18 months. He emphasizes that there is no characteristic picture of bronchial carcinoma and that the first routine screening and radiographs make the diagnosis of bronchial carcinoma certain only in the minority of cases. In the majority of cases the condition can be only suspected. Unilateral, homogeneous, persistent infiltration of lung, after the fourth decade should always arouse suspicion. In advanced cases of this disease other methods may be utilized, such as tomography, bronchography, and, if time permits, "test radiotherapy". The author's

experience is that 82% of bronchial carcinomata originate in the perihilar part of the lung and so cause enlargement of the root shadow. Findings are similar in epithelioid infiltration and chronic perihilar abscess.

Bronchography is one of the best means of diagnosis of bronchial carcinoma. This method has been improved in recent years by introduction of rapidly absorbed media, and by serial bronchography. The author employs a contrast medium which is absorbed in a few hours and so permits the uniform filling of one hemithorax without danger. Bronchography is performed under screening control, and serial films are taken. A constant filling defect is pathognomonic. A routine examination, tomography, and bronchography are carried out in one day if there is a possibility of bronchial carcinoma. Correct diagnosis is obtained with this procedure in the majority of cases. Cases in which doubt persists are re-examined at intervals of not more than 8 days. "Test radiotherapy" with a dose of 60 to 80 r at 2-day intervals, three or four times, is a valuable factor in diagnosis of doubtful infiltrations, but only the complete disappearance of the infiltration excludes a diagnosis of neoplasm. For x-ray diagnosis of inoperability of bronchial carcinoma plain radiography, tomography, and bronchography are needed, special attention being paid to the behaviour of the trachea and oesophagus (filled with barium) and, of course, to any evidence of the presence of metastases.

To confirm or to exclude the presence of metastases all symptoms are investigated by radiography of the relevant part, in order not to overlook skeletal metastases. The possibility of metastases in the brain and in abdominal organs must not be forgotten. The incidence of metastases of bronchial carcinoma is well shown in the report of the Pathological Institute of Graz; out of 150 cases of bronchial carcinoma studied at necropsy, only 6.5% were free from metastases.

The author's routine is to examine the lung fields of patients recommended for x-ray examination because of digestive disturbance. Several cases of bronchial carcinoma were found in which the only symptoms were those relating to the digestive tract. In the author's series of 137 cases there were 60% definitely diagnosed as bronchial carcinoma, 26% probable cases of bronchial carcinoma, and 14% of cases not diagnosed ante mortem.

W. J. Czyzewski

#### 118. The Roentgenographic Appearance of Interatrial Septal Defect. A Report of Twelve Cases

R. F. HEALEY, J. W. DOW, M. C. SOSMAN, and L. DEXTER. *American Journal of Roentgenology and Radium Therapy* [Amer. J. Roentgenol.] 63, 646-656, May, 1950. 8 figs., 15 refs.

The authors present an analysis of 12 cases of interatrial septal defect, all in adult patients examined at the Peter Bent Brigham Hospital, Boston, Massachusetts. The diagnosis was established by means of cardiac catheterization. In all cases there was evidence of a shunting of oxygenated blood from left to right, and only in one case was the net shunt in the reverse direction. In all except this one case the right ventricular output and pulmonary flow were increased. The systemic blood

flow was reduced in all but 2 of the cases. The radiological findings were similar to those described by other observers and included: right atrial and right ventricular enlargement, which in some cases simulated left ventricular enlargement, this being excluded electrocardiographically; enlargement of the main pulmonary artery and its branches; expansile pulsation of the main pulmonary artery and its hilar branches; relative smallness of the aortic knuckle; and absence of demonstrable left atrial enlargement. While a moderate left-to-right shunt through the atria in the absence of pulmonary hypertension may produce no recognizable changes in the radiographic appearance of the heart and great vessels, a small shunt with marked pulmonary hypertension gives rise to appearances such as are found in cases of a large shunt with no pulmonary hypertension. The radiographic appearances in Eisenmenger's complex and cor pulmonale due to primary pulmonary arterial obstruction may be identical with those in interatrial septal defect, while those found in interatrial defect plus mitral stenosis may be indistinguishable from those in cases of mitral stenosis alone, since the left auricular enlargement is the only additional radiological sign found.

G. A. Stevenson

**119. Non-significant Ventricular Shift in Pneumoencephalograms, with Particular Reference to Bowing of the Septum Pellucidum**

D. C. EAGLESHAM. *Radiology [Radiology]* **55**, 1-11, July, 1950. 5 figs., 3 refs.

Asymmetry of the ventricles found on encephalography at the 24-hour examination in cases where no asymmetry was present at the first examination must not be regarded as pathological. The author found such asymmetry at the 24-hour examination in 2% of cases examined in the recumbent position with the central ray vertical. Possibly the incidence of this finding may be different on examination in the upright position.

A. Orley

**120. High-voltage Technic in the Diagnosis of Polypoid Growths of the Colon**

C. GIANTURCO. *Radiology [Radiology]* **55**, 27-29, July, 1950. 6 figs., 6 refs.

The technique favoured by the author for the demonstration of polypoid tumours of the colon is based on the observation that radiographic opacity changes with the voltage employed. Thus for barium-enema examinations a barium mixture is used which is fully opaque at fluoroscopy, but can be made more or less transparent by increasing the voltage for radiography. "This means that the depth of the colon, as well as its surface, can be made visible, just as we see the trabeculation of bone or transparent stones in the gall-bladder." A suitable opaque medium for this purpose is a suspension of one part of barium powder in four parts of water, which is opaque when viewed on the fluoroscopic screen. For radiographic penetration of this medium the factors used by the author are: 100 kV, 300 mA, exposure 0.125 to 0.375 second at 36 inches (91 cm.), with Bucky grid and par-speed screens. With these factors it is possible to visualize one loop of the colon lying behind another and

radiotranslucent areas, which may be caused by polypi, air-bubbles, or faecal matter, become readily visible.

Radiographs must be taken with varying incidence of the central ray and with the patient in various positions. This allows multiple checks to be made of doubtful shadows. Faecal matter is mottled and irregular, air-bubbles tend to be multiple, round or oval, and varying in shape and position on the different films. Polypi may be of any shape and in any position, but remain essentially unchanged in the various views, and in cases of doubt, at a second examination. In order to avoid sedimentation of the barium, fluoroscopy must be carried out rapidly and systematically and the rate of flow kept fairly fast.

A. Orley

**121. Immediate Cholangiography. Indications, Technic and Illustrative Cases**

R. F. CARTER and L. GILLETTE. *Journal of the American Medical Association [J. Amer. med. Ass.]* **143**, 951-954, July 15, 1950. 4 figs., 15 refs.

In the surgical management of difficult and obscure lesions of the biliary tract, the authors advocate the performance of cholangiography at operation as a means of revealing site of obstruction, extent and degree of duct dilatation, and the like. Evidence may thus be furnished which will enable the surgeon to make a better choice of operative technique. Details of the technique of injecting contrast medium either into the gall-bladder or into the ducts are given. An ordinary mobile unit is all that is needed in the way of x-ray plant. Cholangiography is carried out before the biliary tract is incised, except where a catheter or cannula is employed for making the injection. Three cases are reported in which cholangiography was of assistance in showing the site of obstruction. These comprised a case of congenital common-duct stenosis, a case of retained stone in the common duct after cholecystectomy, and a case of common-duct obstruction caused by a remnant of cystic duct which had been left after previous cholecystectomy. The authors consider the procedure to be a simple, safe, and reliable method of determining the exact configuration of anatomical lesions of the biliary tract.

A. M. Rackow

**122. Cystographic Studies in Placenta Praevia**

M. DANNENBERG, J. S. BEILLY, M. B. RODNEY, and C. STORCH. *American Journal of Roentgenology and Radium Therapy [Amer. J. Roentgenol.]* **64**, 53-60, July, 1950. 11 figs., 14 refs.

The authors confirm the value of Ude and Urner's method (*Amer. J. Roentgenol.*, 1934, **31**, 230) of instillation of sodium iodide solution into the bladder in order to confirm a suspected diagnosis of placenta praevia in cases of vertex presentation. Radiographs are taken in the antero-posterior and in both oblique views, and the authors stress the frequent value of the latter. The criteria adopted for the diagnosis of placenta praevia are: (1) high, asymmetrically disposed foetal head; (2) a separation of more than 1 cm. between the shadow of the foetal skull and the outline of the opaque medium in the bladder; (3) asymmetry of the bladder horns;

and (4) a newly-noted sign—rigidity of the bladder, with irregularity of its superior border caused by encroachment of the lower uterine segment.

Out of a total of 104 cases of placenta praevia at the Beth-El Hospital, Brooklyn, N.Y., between 1941 and 1948, cystograms were made in 72 cases and resulted in a correct diagnosis in 55, 36 of these diagnoses being positive for placenta praevia, and 19 negative and subsequently confirmed by uneventful delivery. In 17 cases an incorrect inference was drawn.

[The references given are confined to American sources.]

A. M. Rackow

#### 123. Roentgenkymography of Uterus and Tubes in Sterility. (Рентгенокимография матки и труб при бесплодии)

S. J. SHAKHTMEISTER. *Акушерство и Гинекология [Akush. Ginek.]* No. 3, 55-58, May-June, 1950. 2 figs.

Roentgenkymography of the uterus and tubes was used in the study of 50 cases of sterility. The normal uterus and tubes both contract at a rate of about 12 a minute. In sterile women there is discrepancy between the contractions of the uterus and those of the tubes. While the latter contract 4 or 5 times a minute, the former contracts 6 or 7 times, the most powerful contraction occurring at the fundus. A correlation was also found between the degree of tubal inflammation, tubal patency, and the ability of the tubes to contract. Where inflammation was far advanced, tubal contractions were either greatly reduced or were absent.

E. W. Collis

#### 124. The Radiological Diagnosis of Primary Carcinoma of the Fallopian Tube (with 35% "Perabrodil"). (Die Diagnose des primären Tubenkarzinoms im Röntgenbild (mit 35%-igem Perabrodil))

E. ANTONOWITSCH. *Fortschritte auf dem Gebiete der Röntgenstrahlen [Fortsch. Röntgenst.]* 73, 189-194, June, 1950. 9 figs., 14 refs.

Fallopian-tube carcinoma is rare (0.6% of all female genital carcinomata). It is very malignant, and must therefore be diagnosed as early as possible. Diagnosis is very difficult, and cases are known in which there were no symptoms for 4 to 5 years. Symptoms pointing to malignancy may be obscured by those of simple adnexitis. The author describes the usual history and symptoms (hydrops of the tube, watery discharge, pain radiating to the back, thigh, and navel, and primary sterility, which is present in 60% of cases). The average age is 45 to 50. In younger subjects symptoms may be confused with those of endometriosis. Macroscopically, two types may be differentiated: (1) solid pedunculated tumour; (2) diffuse papillary mucosal tumour.

Since 1942 the author has used a water-soluble contrast medium (35% "perabrodil") for salpingography, because it fills the tubes uniformly, permits good visualization of the mucosal pattern, and passes through even the narrowest parts of the tube. He has by this means diagnosed 2 cases of tubal carcinoma, and believes that he was the first to diagnose this condition by radiography. He suggests that frequent hystero-

grams be taken in patients of the carcinoma age, in order to increase the frequency of early diagnosis of carcinoma.

W. J. Czyzewski

#### 125. Arteriosclerosis and Arterial Thrombosis in the Lower Limb. A Roentgenological Study. [In English] A. LINDBOM. *Acta Radiologica [Acta radiol., Stockh.]* Suppl. 80, 1-80, 1950. 42 figs., bibliography.

The occurrence and distribution of arteriosclerosis and the location of arterial thrombosis in the vessels of the legs were studied in 356 limbs at necropsy, and in 295 limbs during life. The main arteries of both legs in 196 cadavers were injected with contrast medium and radiographed *in situ*. The arteries were then dissected out, treated with formalin, again radiographed, and studied microscopically. Soft-tissue radiographs of the leg were found to give the most information. For the living subjects, the technique was as follows: morphine and scopolamine were given half an hour previously if the patient were in hospital (arteriography was performed on 56 unprepared out-patients without any complication). The injection was made percutaneously into the femoral artery in the groin at a point where pulsation was readily palpable. A needle 6 cm. long and with an inner diameter of 0.8 cm. was used, and at a pressure of 2.5 atmospheres 30 ml. of 35% diodone was injected in 7 seconds, the needle being directed proximally to avoid the risk of injecting the profunda femoris artery only. The injection was followed by a sensation of warmth in the leg. Extravasation of the contrast medium occurred occasionally, with a feeling of tension and sometimes rather severe pain but no other untoward result.

Slight intimal thickening, when present, was most common in the femoral artery above the knee-joint, while that portion of the popliteal artery below the joint was particularly free. The distribution was different when the intimal thickening was more advanced; this indicates, according to the author, that an additional factor must determine its development in the latter case. Constriction of the branches of the main arteries at their origin was a prominent feature. It is stated that intimal calcification, which is a sign of arteriosclerosis and is related to the origin of arterial thrombosis, is radiologically distinct from medial calcification, which has been demonstrated to be dependent on movements of the artery and is hence more commonly found in the vessels below the knee than in the thigh.

The origin of most of the thromboses found in the femoral artery was in the inguinal canal and usually extended proximally. Thrombosis of the profunda femoris was a rare finding and was more frequently located below the knee than in the thigh. It was also more common in the left leg. No explanation of these findings is offered. Intimal haemorrhage appeared to play a great part in the pathogenesis of arterial occlusion, being frequently found at the same site as a thrombosis, thus lending support to the view that the former is a direct cause of the latter. It is suggested that intimal bleeding may be caused by tearing of the sclerotic artery at the sites where the artery is dislocated during movements of muscles and joints.

L. G. Capra



# Pathology

## EXPERIMENTAL PATHOLOGY

### 126. Experimental Allergic Encephalomyelitis. (L'encephalomyélite allergique expérimentale)

B. N. HALPERN, I. BERTRAND, and F. LHERMITTE. *Presse Médicale* [Pr. méd.] 38, 684-687, June 14, 1950. 7 figs., 25 refs.

Experimental allergic encephalomyelitis was induced in monkeys, dogs, and guinea-pigs by the intramuscular injection of a mixture of a suspension of fresh sheep's or rabbit's brain with killed B.C.G., the mixture being sterilized by heating at 60° C. for 45 minutes and then refrigerated. Six monkeys, 19 guinea-pigs, and 3 dogs received weekly doses of 1 ml. intramuscularly. In 5 of the monkeys neurological symptoms appeared on about the 25th day, consisting of paresis of the hind limbs and loss of reflexes and of balance. The condition progressed, with involvement of all limbs, incoordination, and instability, and death followed in about 20 days. One monkey fell into a coma about the 30th day without having shown previous signs of nervous involvement, and died in 5 days. In another a temporary improvement was followed by relapse and rapid progression of the disease. With the guinea-pigs two injections produced symptoms in about 11 days, loss of equilibrium, paralysis of the hind legs, and involuntary and clonic movements being followed by death in about 19 days. Two of the dogs developed similar symptoms after 3 injections. One of the 2 died, but the other had a spontaneous remission, then a relapse, but finally survived.

Microscopically, in the monkeys perivascular inflammatory foci were found throughout the central nervous system in the white matter, with perivascular demyelination and some loss of axis cylinders. In acute cases there was polymorphonuclear infiltration, with some microglial and macroglial elements. In less acute cases there was lymphocytic and plasma-cell infiltration, with gliosis. In some foci venous thrombosis had occurred, with an area of necrobiosis limited by a lymphocytic and glial border and perivascular demyelination. The lesions followed the veins and were limited to the white matter. In the guinea-pig similar lesions were found, though the reaction was less intense. In the dog, however, the cord lesions were more diffuse and confluent, forming localized demyelinating lesions in the anterior and posterior columns.

The mechanism of production of these lesions is discussed. Experiments with suspensions of other organs showed that for encephalitis to result the B.C.G. had to be mixed with brain tissue, and that only white matter was effective. It is suggested that the antigen is a protein molecule and that B.C.G. may act by producing a local reaction preventing the absorption of this antigen and stimulating antibody formation. The formation of antibodies to foreign protein is enhanced by inoculation

into tuberculous animals, but the antibodies from their blood, if injected into other animals, do not give rise to encephalomyelitis. The lesions produced resembled those in such conditions as measles encephalitis rather than those in conditions in which a virus can be demonstrated in the brain, as in rabies, which suggests that the reaction in the former is of an allergic character. The possible relation between this condition and disseminated sclerosis is considered in the light of the findings in the dog.

Gwenvron M. Griffiths

### 127. Experimental "Allergic" Encephalomyelitis. II. On the Nature of the Encephalitogenic Agent

C. E. LUMSDEN. *Brain* [Brain] 72, 517-537, Dec., 1949. 10 refs.

The experiments here reported were undertaken in an attempt to elucidate many different aspects of the problem of experimental encephalomyelitis. In all, 630 guinea-pigs were used and a clear description is given of the standard technique employed and the strict criteria adopted for the diagnosis of positive results. In the first series of experiments a comparison was made between the encephalitogenic activity of homologous and heterologous brain tissue (plus the usual "adjuvants"). Goat and human brain were the heterologous tissues used. The results showed that although an "allergic" encephalomyelitis is induced in guinea-pigs by injection of heterologous brain tissue, this tissue is less potent than homologous brain. In view of the conclusions of other observers that only the white matter of the cortex contains the encephalitogenic factor, injections were made with sterile emulsions of human white and grey matter separately. The author found that both grey and white matter produced an encephalomyelitis, but that the grey matter was more effective than the white. (Of 25 guinea-pigs injected with emulsions of grey matter 12 developed encephalomyelitis, whereas of 25 injected with emulsions of white matter only 4 were affected.) The inference drawn by other workers that the encephalitogenic factor is confined to the white matter and is related to the myelin is therefore refuted. Another series of experiments were carried out with autoclaved and formalinized emulsions in order to determine whether brain tissue which had undergone these processes was still encephalitogenic. The results proved that autoclaved brain tissue is as potent as normal whole brain, but that formalinization, though it does not destroy the encephalitogenic agent, reduces it to some extent. Experiments designed to test the encephalitogenic activity of foetal guinea-pig brain tissue gave interesting results: not only was emulsion of foetal brain highly effective in producing encephalomyelitis, but the peak of the disease was reached, on an average, 10 days earlier than in guinea-pigs treated with adult guinea-pig brain. The author considers that this finding reflects

not so much an earlier onset of the disease as its more rapid evolution.

In order to ascertain whether tissues other than those of the nervous system contain the encephalitogenic factor, emulsions of liver, spleen, kidney, adrenal, testis, placenta, and acetone-dried skin were each injected into a series of 25 animals. All results were negative except that one animal, injected with emulsion of skin, developed definite paralysis, with histological evidence of encephalomyelitis. In view of this finding, another series of 25 animals were injected with emulsion of skin. This time a uniformly negative result was obtained and the single positive result in the previous series was therefore ignored. The effect of a smaller dosage of an encephalitogenic emulsion was the subject of another series of experiments, it being found that one-tenth of the standard dosage of the emulsion was equally effective.

Extraction of guinea-pig brain with acetone, alcohol, ether, and chloroform was carried out and it was found that the brain residues after extraction with these solvents were as potent as whole brain in inducing encephalomyelitis. Finally, experiments were carried out to determine the immunizing factor which protects animals against subsequent injections with an encephalitogenic agent. Two series of guinea-pigs, one previously treated with a cold alcoholic extract of brain and "adjuvants", the other series with an emulsion of adrenal gland, plus "adjuvants", which had proved negative, were given five weekly injections of a potent emulsion of fresh guinea-pig whole brain with "adjuvants". This emulsion had proved highly encephalitogenic in control animals. Only one animal of the 40 in the two series developed encephalomyelitis, and the author infers from this result that the immunizing factor is contained in the "adjuvants".

[The scope of these experiments was wide, and involved much careful planning as well as technical skill. The lucid exposition of the results obtained deserves commendation, and might well be studied by other experimentalists.]

Ruby O. Stern

#### 128. Experimental Vascular Disease due to Desoxycorticosterone and Anterior Pituitary Factors. II. Comparison of Pathologic Changes

G. M. C. MASSON, J. B. HAZARD, A. C. CORCORAN, and I. H. PAGE. *Archives of Pathology* [Arch. Path.] 49, 641-664, June, 1950. 6 figs., 37 refs.

In order to compare forms of experimental hypertension produced by different means, albino rats were divided into six groups, three experimental and three control, in experiments performed at the Cleveland Clinic Foundation. In the first group, one or both kidneys were wrapped in silk, and in some cases unilateral nephrectomy was performed. Death from renal insufficiency was particularly common in animals with only one kidney (this being wrapped in silk), and hypertension soon appeared in these. The degree of atrophy did not seem to be parallel to the rise in blood pressure. The atrophic kidneys contained no abscesses, had a granular surface, and were large and greyish with an irregular surface and small white and haemorrhagic

points. Lesions frequently developed in the splanchnic arteries.

In a second group, female rats after unilateral nephrectomy received 2.5 mg. deoxycortone acetate in water by subcutaneous injection daily, and 1% sodium chloride solution to drink. In the third group, unilaterally nephrectomized rats were given injections of a crude suspension of powdered anterior pituitary gland. The daily dose was either kept constant or raised; in the latter case the dose was 20 mg. for 13 days, 40 mg. for 10 days, and then 60 mg. for the rest of the experiment.

Nephrosclerosis was present in every group, the lesions and hypertension being produced most rapidly and most consistently in the second group, and least regularly in the third. In the kidney the tubules were dilated and often contained erythrocytes and hyaline casts. Most of the glomeruli were large and anaemic and their capsular spaces were obliterated or contained casts. The tufts were often necrotic and hyaline. A necrotizing arteritis developed both in the kidneys and elsewhere.

The authors think that these lesions are the result and not the cause of the hypertension and that they are identical with and correspond to those of human malignant nephrosclerosis.

Peter Harvey

#### 129. A Factor in Neutralized Human Gastric Juice which Prolongs Survival of Gastrectomized Rats

D. C. BALFOUR, G. M. HIGGINS, and K. A. WOODS. *Proceedings of the Staff Meetings of the Mayo Clinic* [Proc. Mayo Clin.] 25, 434-441, July 19, 1950. 3 figs., 16 refs.

Rats generally survive 6 months to one year after experimental removal of the stomach, a gain in weight for 2 to 3 months after operation being followed by a decline in weight leading to death. During this decline a microcytic hypochromic anaemia develops, resistant to liver and folic-acid therapy, which is changed by the administration of iron into a macrocytic hypochromic anaemia. It has been shown that the loss of weight is not due to factors such as lack of vitamins, liver, or iron, or to the fact that the rat begins to select proportionately less protein from its food after the operation.

The authors report that the administration of neutralized human gastric juice to gastrectomized rats caused them to gain in weight compared with the controls. The anaemia was not affected, and when the haemoglobin level fell to 8 g. per 100 ml. of blood, the animals began to lose weight. At this stage the administration of ferric citrate, if given within 12 weeks of the last dose of gastric juice, caused an increase in the weight of the animals. The resumption of gastric-juice therapy together with the iron led to further gains in weight. Seventy weeks after operation all the treated animals were alive and well, with an essentially normal blood picture.

The authors point out that a hypochromic microcytic anaemia may be related to abnormal protein metabolism, and certainly gastrectomized rats show a decreased intake of protein. It is suggested that a factor or factors contained in neutralized human gastric juice may be related to normal protein synthesis.

P. Mestitz

## 130. The Endocrine Kidney. [In English]

M. SIMONSEN. *Acta Pathologica et Microbiologica Scandinavica* [Acta path. microbiol. scand.] 27, 520-536, 1950. 9 figs., 10 refs.

Selye's concept of the "endocrine kidney" is based on the changes occurring in the kidneys of rats subjected to a modification of the Goldblatt procedure in which the aorta is constricted between the two renal arteries. The left kidney, whose artery comes off the aorta below the right, is thereby rendered ischaemic, together with the hind-part of the body, and the rats die of hypertension in 2 to 3 weeks. Histologically, the left kidney shows loss of the glomeruli and tubules of the outer cortex and active proliferation of the tubular cells of the inner cortex. Selye regards these surviving tubular cells as the source of a pressor substance secreted by the kidney, this endocrine function remaining, or even increasing, after the kidney had lost all excretory function. The author repeated Selye's work, and succeeded in producing malignant hypertension in 12 rats and benign hypertension in 5. In only one of these 17 rats did the left kidney show a picture identical with Selye's description of that of the "endocrine" kidney, and in this case the author interprets the changes as degenerative, regarding the apparent proliferation of the tubular cells as desquamative in nature. The remaining 16 kidneys all showed the changes usually seen in Goldblatt kidneys—degeneration, necrosis, fibrosis, and infiltration with lymphocytes and histiocytes. Casts were present and groups of tubules were filled with desquamated cells. Changes in the visceral arteries and arterioles which were similar to those found by Selye are also described and illustrated. The author concludes that Selye's "endocrine kidney" must be regarded as a histological curiosity caused by a certain degree of arterial constriction, but "nothing seems to indicate that it takes up any exceptional position with regard to the production of pressor substances."

I. Doniach

## 131. The Pathogenesis of Hypertension Induced by Renal Constriction

L. J. RATHER. *Journal of Experimental Medicine* [J. exp. Med.] 92, 59-76, July, 1950. 13 figs., 21 refs.

In a series of experiments performed at Stanford University School of Medicine, San Francisco, groups of 10 or 12 young male rats were kept on a standard diet and subjected to the following procedures designed to cause hypertension: (a) unilateral nephrectomy with exposure and handling of the other kidney; (b) unilateral nephrectomy with constriction of the other kidney by a figure-of-eight ligature; (c) unilateral nephrectomy and removal of both poles of the opposite kidney; (d) exposure and handling of one kidney and constriction by ligature of the other. The rats' blood pressure was measured frequently under ether anaesthesia before and after these operations. After 50 days the rats were killed and the weights of cardiac and renal tissue determined, sections of various tissues examined, and blood haematocrit and creatinine values ascertained.

Rats in group (b) developed hypertension 4 days after operation, but the animals in the other groups did not.

No correlation was found between the mass of functional kidney, as indicated by the weight of wet renal tissue post mortem or the serum creatinine level, and the degree of hypertension, nor between blood pressure and heart weight. Interference with kidney growth could not be related to the development of hypertension, since the blood pressure of animals in group (d) remained normal despite the restrictive effect of the ligature on one kidney. In group (c) there was a significant increase in the weight of the heart which seemed to be related to the presence of some degree of anaemia in these animals, but not to the blood pressure, which was normal. Apart from the restriction in growth of the ligated kidneys in group (d), the only significant difference found in the kidneys as between the various groups was the presence of hypertrophy of the media of the small renal arteries in group (b).

It is concluded that renal constrictive hypertension in rats is due to interference with renal haemodynamics or tissue tensions leading to the release of some pressor substance by the affected kidney, and not to reduction in the amount of functional renal tissue, constriction of the pedicle, or interference with compensatory hypertrophy after unilateral nephrectomy.

James D. P. Graham

## 132. Diabetic State with Lipaemia and Hydropic Changes in the Pancreas Produced in Rabbits by Cortisone

S. D. KOBERNICK and R. H. MORE. *Proceedings of the Society for Experimental Biology and Medicine* [Proc. Soc. exp. Biol., N.Y.] 74, 602-605, July, 1950. 1 fig., 4 refs.

This work is reported from the Pathological Institute of McGill University. After a suitable period of observation 2 rabbits were given two intramuscular injections of 10 mg. of cortisone acetate daily, and on the third day were placed in a room where the temperature varied between  $-1^{\circ}\text{C}$ . and  $-13.3^{\circ}\text{C}$ ., being nearer the lower limit most of the day. On the sixth day each animal received, intravenously, 10 ml. of horse serum per kg. body weight. In the same room were kept pairs of control animals which received either no treatment or horse serum only. Unlimited food and water were provided. (The authors now believe that similar results would have been obtained if the animals had been kept at normal room temperature.)

Five days after the commencement of cortisone administration an increase in its lipid content caused definite cloudiness of the serum and there was a rise in the blood sugar level, with glycosuria. Although necropsy on one animal which died on the 12th day was not performed until approximately 18 hours after death, the authors feel that post-mortem change could not have been significant in the cold room. The islets of Langerhans showed some swelling of the cells and occasional fragmentation of the cell border. In an animal killed on the 22nd day of cortisone treatment, immediate necropsy showed "hydropic change" of the cells of the islets and ductules of the pancreas. The hydropic cells contained glycogen stainable with Best's carmine. Gomori's stain showed the vacuolation to be chiefly in the  $\beta$ -cells. Microscopically, these pancreatic



lesions resembled those seen in naturally-occurring and experimentally-induced diabetes. The authors wonder whether the lipaemia was due to the cortisone or secondary to the disturbance of carbohydrate metabolism.

Peter Harvey

**133. The Effect of Anti-Rh Serum on Cultures of Human Embryo Tissues, Nervous and Splenic.** (Effet du sérum anti-Rh sur les tissus embryonnaires humains nerveux et splénique en culture)

G. BARSKI and A. EYQUEM. *Annales de l'Institut Pasteur [Ann. Inst. Pasteur]* 9, 44-50, July, 1950. 3 figs., 20 refs.

The growth of cells from the human embryo is much less rapid in anti-Rh serum than in normal human serum. In human embryo spleen cultures in anti-Rh serum there is agglutination of erythrocytes, accompanied by very active phagocytosis and the development of very numerous giant cells of the Langhans type.

G. M. Findlay

**134. Endogenous Neoplasm-inducing Substances in Organs of Leukaemic Human Subjects.** (О бластомогенных веществах в тканях больных лейкозом)

M. O. RAUSCHENBACH. *Архив Патологии [Ark. Patol.]* 12, No. 3, 9-15, May-June, 1950. 6 figs., 7 refs.

Benzene extracts of liver, spleen, lymph nodes, bone marrow, brain, bile, and urine of subjects dying of chronic myeloid and lymphoid leukaemia, of acute leukaemia, and of myeloma were prepared according to the method described by Kleinenberg, Neufach, and Schabad. Only specimens taken not later than 30 hours after death were used, and the yield of substances extracted, after removal of the benzene, varied from 2 to 15 g. for each 1 kg. of tissue. Two-month-old mice of low-breast-cancer strains were used and an average of 2 to 3 g. of each extract was injected into groups of 5 or 6 mice, each mouse receiving, at intervals of 10 to 12 days, 4 to 7 subcutaneous injections of 0.3 g. of the extract diluted two or three times in rabbit or dog fat. Extracts of organs from 7 persons killed in street accidents and from 4 who died of cancer were used as controls.

Of 162 mice treated with extracts of the organs of leukaemic subjects and surviving for at least 4½ months, 46 developed tumours at the site of injection and 16 developed tumours at distant sites. In addition, 8 mice developed leukaemia. The tumours were classified as spindle-celled and polymorphic-celled sarcomata. Some of the sarcomata were successfully transplanted for 3 to 8 generations. Eleven of the tumours at distant sites were classified as adenocarcinoma, 2 as lymphosarcomata of the mediastinum, 2 as lung adenoma, and one as myeloma in the region of the kidneys. Of 18 mice injected with extracts of the liver of cancerous subjects and surviving for at least 6 months, 7 developed tumours (5 of them at the site of injection) and 2 leukaemia. In the group of 37 mice surviving 6 months after the injection of liver extracts from persons killed in street accidents, only one developed an adenocarcinoma of the mammary gland.

All the extracts tested from cases of acute and chronic leukaemia were found to contain neoplasm-inducing substances. Ten mice injected with extracts of organs of subjects dying of leukaemia or cancer developed myeloid leukaemia, with changes in the liver, spleen, bone marrow, and blood. Successful transplantation of the leukaemias is reported. Mice of the two strains used had not previously been observed to develop spontaneous leukaemia. The author concludes that acute and chronic leukaemia and cancer may have a similar origin.

L. Dmochowski

**135. Pathology of Leukaemia Induced in Mice with Extracts of Organs of Leukaemic Human Subjects.** (Патологическая анатомия экспериментального лейкоза, полученного при введении бензольных экстрактов из органов больных, умерших от лейкоза)

M. P. CHOCHLOVA. *Архив Патологии [Ark. Patol.]* 12, No. 3, 16-22, May-June, 1950. 4 figs., 3 refs.

Groups of mice were injected with extracts of different organs from human subjects dying of various neoplastic diseases, as follows: (1) chronic myeloid leukaemia (4 cases); (2) chronic lymphoid leukaemia (3 cases); (3) acute leukaemia (4 cases); (4) multiple myeloma (1 case); and (5) cancer of the stomach (4 cases). A control group received injections of extracts of organs from healthy subjects who had died in accidents.

Four out of 75 animals in the first group developed leukaemia, with cells of the myeloblast and myelocyte type present in the liver, spleen, bone marrow, and blood. All 4 animals had spindle-celled sarcomata at the site of injection of the extracts. The tumours and leukaemia were successfully transplanted and all mice into which the tumours were transplanted developed myeloid leukaemia. Nine mice of the 36 in the second group showed tumours at the site of injection, and 7 had tumours at distant sites. In several mice slight lymphocytic infiltration of the liver and hyperplasia of the spleen and lymph nodes were observed, but not classified as leukaemia. On transplantation, however, the tumours induced leukaemic changes of the myeloid type in all the recipient mice. In the third group, 10 of the 32 surviving mice developed sarcomata at the site of injection and one at a distant site, and in 3 animals leukaemic changes and sarcomata were observed at the same time. In these 3 mice haemocytoblasts, myeloblasts, and myelocytes were found in the blood. Transplantation of these leukaemias was again successful. Five animals of the 19 in the 4th group developed sarcomata at the site of injection, and 4 at distant sites, while one developed myeloid leukaemia. Seven out of 18 mice in the 5th group developed sarcomata and 2 myeloid leukaemia. No leukaemic changes were found in the controls.

Altogether 8 out of 162 mice (4.9%) developed myeloid leukaemia with changes in the liver, spleen, lymph nodes, bone marrow, and blood. Diffuse hyperplasia and myelosis were found in the bone marrow and spleen, with only local changes in the lymph nodes. Extramedullary blood formation was found in the liver, along the capillaries and Glisson's capsule. The presence of segmented leucocytes with myelocytes and myeloblasts

was observed both in the bone marrow and in internal organs. Enlargement of the liver and spleen, however, was usually the result of amyloidosis. Only the myeloid type of leukaemia was observed. Extracts of liver from subjects with chronic myeloid leukaemia induced the highest incidence of leukaemia in mice (5.3%). Extracts of liver, spleen, lymph nodes, and lung from subjects with chronic lymphoid leukaemia induced no leukaemic changes, but tumours which, on transplantation, led to the development of myeloid leukaemia in mice. Extracts of bile and brain from cases of acute leukaemia induced leukaemia in mice, with an increase in the number of leucocytes and myeloblasts and myelocytes present in the blood. The diagnosis of leukaemia was only made if diffuse growth of myeloid tissue, with infiltration of the organs and changes in the blood, was observed. These changes are considered to be similar to those induced in mice by carcinogenic hydrocarbons.

L. Dmochowski

### 136. The Effects of a Transplanted Granulosa-cell Tumor on Mice in Parabiosis

J. T. WOLSTENHOLME. *Cancer Research* [Cancer Res.] 10, 344-347, June, 1950. 6 figs., 13 refs.

Mice bearing transplanted granulosa-cell tumours were united in parabiosis to non-tumour-bearing mice, to determine whether the observed systemic effects of this tumour would appear in the parabiotic partner. The tumour used arose from the homologous graft of an ovary into the pancreas of an ovariectomized mouse of the C57 black strain, and had been through five serial passages in C57 mice. Implants of this tumour were then made subcutaneously in mice of the same strain, and as soon as a growth was palpable they were joined in parabiosis to litter-mates, 11 out of 12 of these pairs being subjected to ovariectomy before the union. The pairs were killed after periods ranging from 11 to 110 days. At necropsy the tumour-bearing mice showed the changes usually associated with this type of tumour—grossly enlarged liver and spleen, dilated heart, dilated liver sinusoids, engorgement of the spleen, and dilated sinusoids at the cortico-medullary junction in the adrenals. None of these changes was found in the partners. The tumours also had oestrogenic effects on the mice bearing them, but not on the partners.

In discussing these findings, the author relates them to the observed facts that erythrocytes or dyes injected into one of a parabiotic pair soon appear in the other, but that the blood concentration of oestradiol injected into one parabiotic partner must be increased to forty times the effective level before its effects can be observed in the other. It is concluded that the systemic effects of this tumour are unlikely to be due to an infective agent.

M. H. Salaman

### 137. Perihepatitis and Adhesive Peritonitis in Mice following the Intraperitoneal Injection of Mercurial Preparations

H. FALCONER and E. H. DERRICK. *Journal of Pathology and Bacteriology* [J. Path. Bact.] 62, 341-350, Oct., 1950. 15 figs., 2 refs.

See also Section Radiology, Abstract 104.

## MORBID ANATOMY

### 138. Changes at the Lung Hilum with Age. (Über Altersveränderungen am Lungenhilus)

W. BOHN. *Virchows Archiv für Pathologische Anatomie* [Virchows Arch.] 318, 289-308, 1950. 7 figs., 28 refs.

The slaty induration of the lung hilum seen at necropsy on old people without a history of special exposure to dust was studied in 27 cases. The changes were the more distinct the older the patient; they proved very similar to those described in true silicosis. As well as changes in the bronchial lymph nodes, alterations were found in the bronchi and in the vessels. The changes in the bronchi—bronchitis deformans—consisted of a walling in of the structure with areas of destruction and of deposition of cartilage and consequent deformation of the lumen; destruction of mucous glands, with danger of ascending infection, was also present. The vessels were, in a similar way, surrounded by a sclerotic wall, and showed callosities and rigidity of the wall and narrowing of the lumen. These changes may be explained as silicotic and partly tuberculous in origin.

O. Neubauer

### 139. Bronchogenic Carcinoma: a Study of 60 Necropsies

I. M. REINGOLD, R. E. OTTOMAN, and B. E. KONWALER. *American Journal of Clinical Pathology* [Amer. J. clin. Path.] 20, 515-525, June, 1950. 7 figs., 18 refs.

At the U.S. Veterans Administration Hospital, Birmingham, Alabama, during a period of 3½ years, 85 cases of carcinoma of the bronchus were diagnosed. All these patients died within 1 year of diagnostic biopsy, irrespective of cell type, and 60 were examined post mortem. The tumour in 39 of these cases was hilar, in 19 peripheral, and in 2 diffuse; in 40 it was a squamous-celled carcinoma, in 18 undifferentiated, and in 2 it was an adenocarcinoma. This last type is five times more common in women, but in the present series there was inevitably a preponderance of male patients. During this period carcinoma of the bronchus was the most common malignant tumour encountered at the hospital and constituted 30% of malignant neoplasms found at necropsy. One case of squamous carcinoma arose in association with bronchiectasis, but this condition is not generally regarded as precancerous.

D. M. Pryce

### 140. A Histological Study of Hanot's Biliary Cirrhosis.

(Contribution à l'étude histologique de la maladie de Hanot)

Y. POURSIÈRES, R. POINSON, and R. MATHIEU. *Annales de Médecine* [Ann. Méd.] 51, 197-222, 1950. 15 figs.

A detailed report is given of a case of Hanot's cirrhosis in an Armenian woman, aged 46, who had recurrent attacks of right-sided abdominal pain and jaundice following cholecystectomy. An enlarged axillary lymph node was removed, and liver biopsy was performed at a subsequent splenectomy. The patient died a year later, when a detailed histological examination of all the tissues was made. The authors produce evidence of a generalized mesenchymal affection of the liver, kidney,

spleen, lymph nodes, and lung, and suggest that the individual liver cells are damaged and the Kupffer cells stimulated to hyperplasia and metaplasia. They can suggest no causal explanation for the pathological process resulting in a monolobular cirrhosis.

E. T. Ruston

### CLINICAL PATHOLOGY

#### 141. Chymotrypsin Inhibition by Human Serum in Health and Disease

H. TAUBER. *Proceedings of the Society for Experimental Biology and Medicine* [Proc. Soc. exp. Biol., N.Y.] 74, 486-489, July, 1950. 7 refs.

Details are given of a method of estimating the amount of chymotrypsin inhibitor in blood serum, using as substrate homogenized milk buffered at pH 5.0. In a study of 1,556 patients, including 60 with malignant neoplasia, abnormal values (increased amount of chymotrypsin inhibitor) were found in only 3.8% of patients with non-malignant diseases, and nearly half of these were cases of pregnancy of over 15 weeks' duration. The percentage of abnormal values was much higher in patients with cancer. Although the antichymotrypsin content of serum is not changed in early malignant disease, the test may, however, assist in the diagnosis of advanced malignancy and in the detection of hidden metastatic cancer.

L. A. Elson

#### 142. A New Hyaluronidase Test Based on the Erythrocyte Sedimentation Rate. (Nowa metoda oznaczania in vitro hialuronidazy oparta na zjawisku opadania krwinek)

B. ZABLOCKI. *Polski Tygodnik Lekarski* [Polsk. Tyg. lek.] 5, 521-524, April 3, 1950. 15 refs.

The author's method for the quantitative estimation of hyaluronidase is based on the effect of hyaluronic acid in raising the erythrocyte sedimentation rate (E.S.R.). The influence of hyaluronic acid on the E.S.R. is pronounced both in normal persons and in patients suffering from various diseases in which the rate is usually increased, but its effect is reduced by treatment with fluids containing hyaluronidase. The minimum accelerating dose of hyaluronic acid was estimated and found to be 0.05 mg. per ml. of citrated blood. For the estimation of hyaluronidase this quantity of the acid is mixed with a constant volume of various dilutions of the specimen under investigation. After 30 minutes' incubation at 37° C. 1.5 ml. of citrated blood is added to each tube and the E.S.R., together with that of several control specimens, determined (after one hour). The titre of hyaluronidase in the fluid examined is calculated from the dilution at which the hyaluronic acid is deprived of its accelerating activity.

According to the author, this new method possesses the following advantages: (a) it is accurate and technically easy, (b) the time required is just over 1½ hours, and (c) the only materials required are 10 ml. of citrated blood and a 0.25% solution of hyaluronic acid in saline.

[The original paper should be consulted for technical details.]

J. W. Czekalowski

#### 143. Total Base Determination in Biological Fluids by Electrodialysis using a New Type of Permanent Aluminium Oxide Filter

O. J. MALM. *Scandinavian Journal of Clinical and Laboratory Investigation* [Scand. J. clin. Lab. Invest.] 2, 92-101, 1950. 2 figs., 22 refs.

#### 144. A New Apparatus for Determination of Total Base by Electrodialysis

M. U. TSAO. *Scandinavian Journal of Clinical and Laboratory Investigation* [Scand. J. clin. Lab. Invest.] 2, 102-105, 1950. 1 fig., 5 refs.

#### 145. Serum Mucoproteins in Children in Health and Disease with Special Reference to Rheumatic Fever

V. C. KELLEY, R. A. GOOD, and I. MCQUARRIE. *Pediatrics* [Pediatrics] 5, 824-835, May, 1950. 4 figs., 25 refs.

In this survey the serum mucoprotein values were calculated from the tyrosine content of the filtrate after adding perchloric acid to blood. There were 107 normal subjects and 207 patients suffering from a wide variety of diseases. In active rheumatic fever the level of mucoprotein in serum was invariably raised up to three times the normal, but fell to normal as activity subsided; close correlation with the erythrocyte sedimentation rate was found. The same applied to rheumatoid arthritis. When chorea was the only sign, values were normal or slightly raised, as also in cases of rheumatic fever in the inactive phase and in uncomplicated streptococcal disease of the throat. In normal children the figures were essentially the same as in healthy young adults. Marked elevation of serum mucoprotein level was encountered in some acute infections and in disseminated malignant disease. The values were consistently low in the lipid nephrosis syndrome.

W. S. Killpack

#### 146. Erythrocyte Sedimentation and Plasma Viscosity Tests in Rheumatic Patients undergoing Spa Treatment

J. E. DAWSON and H. B. SALT. *British Journal of Physical Medicine* [Brit. J. phys. Med.] 13, 152-156, July, 1950. 8 refs.

Simultaneous estimation of the corrected erythrocyte sedimentation rate (C.S.R.) by Collins's method and of the plasma viscosity (P.V.) by the method of Woodmansey and Wilson were made at weekly intervals for 3 weeks in a series of 63 patients with chronic rheumatic conditions in order to assess the sensitivity of these tests as indices of progress in patients undergoing spa treatment. Statistical analysis was made of the technical accuracy of the two methods, and only changes of more than double the widest limits of variation were regarded as significant. Detailed analyses, in five tables, are given of the results, from which it is concluded that the C.S.R. is "sufficiently sensitive to reveal slight changes in a patient's condition sometimes, but not always, associated with small degrees of clinical change". The P.V. was found to be a less sensitive test [during the relatively short period over which the patients were observed]. Note is made of the "diagnostic purposes" of these tests [although there is no elaboration of the diagnostic



inferences to be deduced except in so far as they provide an indication of "abnormality"] and it is recommended that both tests be applied for such purposes. In most cases a close correlation was found between the results of the two tests. When this did not occur it was found that the C.S.R. gave a more reliable indication of the degree of activity in mild early cases of rheumatic disease, while the P.V. results were more dependable in severe cases of long duration.

Harry Coke

147. **A Photoelectric Method for the Determination of Red Cell Numbers and Haemoglobin in Peripheral Blood**  
R. OSMOND and J. S. ROBERTSON. *Medical Journal of Australia* [Med. J. Aust.] 2, 36-40, July 8, 1950. 2 figs., 30 refs.

The superiority of the photo-electric colorimeter over the human eye for colour matching in haemoglobin estimations is well established, but little work has been done on the adaptation of this technique to the counting of erythrocytes. The authors' method is to use venous blood collected into a dry citrated bottle. [The use of Heller and Paul's dry oxalate mixture would have been open to fewer theoretical objections.] To 50 c.mm. of the blood diluted with 0.45 ml. of a stock erythrocyte counting fluid (containing mercuric chloride 0.25%, sodium sulphate 2.5%, and sodium chloride 0.5% in distilled water) 9.5 ml. of 2.5% saline is added and 2 ml. of the resulting suspension is transferred to an absorptiometer tube. An "Ilford 205" red filter is used and the mixed diluting fluids provide the standard. The authors claim a time of 2 to 4 minutes and an accuracy to within 200,000 cells per c.mm. The haemoglobin value can also be determined on the same sample by the addition of 5% caustic soda and the use of a blue filter.

[The adoption of a method such as this for counting erythrocytes would represent a great economy in time and skilled technicians. Not only is the accuracy claimed much greater than that usually obtained (see Biggs and Macmillan, *J. clin. Path.*, 1948, 1, 288, which is quoted in the text, but omitted from the list of references), but the speed is anything up to six times faster than the counting-chamber method. The only serious disadvantage, as the authors point out, is that in blood diseases causing extreme variations in erythrocyte size the error of the method is increased.]

A. Michael Davies

148. **Sternal Marrow Puncture: the Dilution with Peripheral Blood as Determined by P<sup>32</sup> Labelled Red Blood Cells**

N. I. BERLIN, T. G. HENNESSY, and J. GARTLAND. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] 36, 23-28, July, 1950. 1 fig., 7 refs.

149. **A Simple Method for Estimating Albumin-Globulin Ratios in Human Blood Serum.** (Eine einfache Methode zur Bestimmung des Albumin-Globulinverhältnisses des menschlichen Blutserums)

G. W. SCHMIDT. *Zeitschrift für die Gesamte Experimentelle Medizin* [Z. ges. exp. Med.] 115, 651-654, 1950. 2 figs., 7 refs.

150. **Clinical Studies on Blood Coagulation, with a Note on Dicumarol Therapy of Cardiac Diseases.** (Über klinische Koagulationsuntersuchungen mit einem Beitrag zur Dicumaroltherapie der Herzkrankheiten)  
J. JÜRGENS. *Zeitschrift für Klinische Medizin* [Z. klin. Med.] 146, 516-534, 1950. 6 figs., bibliography.

151. **Determination of Circulating Red Cell Volume by Radioactive Chromium**

S. J. GRAY and K. STERLING. *Science* [Science] 112, 179-180, Aug. 11, 1950. 1 fig., 9 refs.

152. **Estimation of Chlorides in Cerebrospinal Fluid in the Diagnosis and Management of Tuberculous Meningitis.** (Le dosage des chlorures du liquide céphalo-rachidien dans le diagnostic et la conduite du traitement des méningites tuberculeuses)

J. TAPIE, J. MONNIER, A. DELAUDE, and —. GONTIER. *Presse Médicale* [Pr. méd.] 58, 809-810, July 15, 1950.

This report from Toulouse is based on a study of cerebrospinal fluid from 50 patients with tuberculous meningitis treated with streptomycin. The value of estimation of the chloride level in the diagnosis and treatment of the disease and in the detection of relapses is underlined. An initial low level and, especially, a progressive fall in the absence of treatment provide strong presumptive evidence of tuberculous meningitis. The number of intrathecal injections necessary can be determined by the changes in the chloride content of the fluid. Intrathecal injections may be stopped when the level is normal, but general treatment must continue until the cell count of the fluid is also normal.

A. Wynn Williams

153. **The Zinc Turbidity Test and its Clinical Application**

R. SCHMID. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] 36, 52-65, July, 1950. 3 figs., 26 refs.

This paper from the University of Minnesota Hospitals gives a fairly exhaustive analysis of the value, or rather the lack of value, of the zinc-turbidity test of Kunkel (*Proc. Soc. exp. Biol.*, N.Y., 1947, 66, 217) in 35 healthy persons and several hundred patients with a variety of hepatic and non-hepatic diseases. In the 35 normal subjects and 159 patients with no evidence of hepatic disease no correlation could be found between the serum gamma-globulin level and the result of the zinc-turbidity test. Thymol-turbidity and cephalin-cholesterol tests performed on 164 patients with liver dysfunction also showed little or no correlation with the zinc-turbidity test. There was no correspondence between the result of this test and the serum bilirubin level in 355 patients, nor was it of use in the differential diagnosis of 57 cases of jaundice.

A. Michael Davies

154. **Bromsulphalein Liver Function Test in Severe Infantile Gastroenteritis. Experimental Studies on Functional Capacity of the Liver in Infants.** [In English]  
J. KAHTIO. *Annales Medicinae Experimentalis et Biologiae Fenniae* [Ann. Med. exp. Biol. fenn.] 28, Suppl. 5, 1-115, 1950. 11 figs., bibliography.

# Microbiology

## VIRUSES

155. A Viral Agent Isolated from a Case of "Non-paralytic Poliomyelitis" and Pathogenic for Suckling Mice; its Possible Relation to the Coxsackie Group of Viruses

F. S. CHEEVER, J. B. DANIELS, and E. F. HERSEY. *Journal of Experimental Medicine* [J. exp. Med.] 92, 153-167, Aug., 1950. 12 refs.

Stools from a group of 19 patients in Worcester, Mass., suffering from non-paralytic poliomyelitis, were injected intraperitoneally into suckling mice, 1 or 2 days old. In 17 instances no pathological changes appeared, but in 2 cases symptoms developed in the mice. Two strains of virus (Powers and Matulaitis) were isolated in this way, one of which, Powers, was studied in greater detail. Only suckling mice and possibly one-day-old voles proved to be susceptible, and no infection of embryonated eggs was produced. In mice infected by the intraperitoneal route after an incubation period of 2 to 3 days, slight tremors, cyanosis, and gasping respiration occurred, being followed by death in 48 hours. The virus was present in both brain and carcass of the mice. Post mortem, myocarditis, adipositis, pancreatitis, hepatitis, and encephalomyelitis could be demonstrated. It is probable that the virus was responsible for the illness of the patient from whom it was derived because there was a rise in titre of complement-fixing antibody and neutralizing antibody for this virus during the illness, but the antibodies were relatively common even in control sera.

There is evidence that the virus is closely related to the Coxsackie group of viruses, but no serological relation to the Connecticut 5, Ohio R, and High Point strains could be demonstrated.

R. Hare

156. Lesions Caused in Suckling Mice by Certain Viruses Isolated from Cases of So-called Non-paralytic Poliomyelitis and of Pleurodynia

A. M. PAPPENHEIMER, J. B. DANIELS, F. S. CHEEVER, and T. H. WELLER. *Journal of Experimental Medicine* [J. exp. Med.] 92, 169-189, Aug., 1950. 21 figs., 19 refs.

A study of the pathological changes produced in suckling mice by the Powers, Matulaitis, De Mole, Kine, McCarthy, Connecticut 5, Ohio R, High Point, WS No. 4, EMC, and Columbia SK viruses of the Coxsackie group was made. The following conclusions were reached.

(1) High Point virus has a predilection for skeletal muscle and produces no noteworthy changes in other organs. (2) Powers, De Mole, Kine, McCarthy, and Connecticut 5 viruses have no effect on skeletal muscle, but produce marked changes in myocardium, liver, pancreas, adipose tissue, and the central nervous system. (3) Ohio R., WS No. 4, and Matulaitis viruses produce lesions in both skeletal muscles and viscera. (4) EMC

and Columbia SK viruses produce lesions in muscle and central nervous system, but none in the viscera.

R. Hare

157. Attempts to Cultivate Rabies in a Cell-free Medium

R. KIRK, M. E. HASEEB, and A. T. DAVIS. *Journal of Tropical Medicine and Hygiene* [J. trop. Med. Hyg.] 53, 167-170, Aug., 1950. 4 refs.

In attempts to cultivate the infective agent of rabies in a cell-free medium by the methods described by Veeraghavan we have failed to demonstrate any multiplication of the virus by using intracerebral titrations in mice for the estimation of virus titres before and after cultivation for 24 hours.—[Authors' summary.]

158. Electrophoretic Studies of Virus-Red Cell Interaction: Mobility Gradient of Cells Treated with Viruses of the Influenza Group and the Receptor-destroying Enzyme of *V. cholerae*

G. L. ADA and J. D. STONE. *British Journal of Experimental Pathology* [Brit. J. exp. Path.] 31, 263-275, June, 1950. 22 refs.

159. Electrophoretic Studies of Virus-Red Cell Interaction: Additive Effect of Viruses of the Influenza Group and the Receptor-destroying Enzyme of *V. cholerae*

J. D. STONE and G. L. ADA. *British Journal of Experimental Pathology* [Brit. J. exp. Path.] 31, 275-284, June, 1950. 1 fig., 6 refs.

160. The Effect of Bacteria, Bacterial and other Polysaccharides, and Various Macromolecular Substances on Influenza Infection in Mice and on Haemagglutination by Influenza Viruses and Chemical Agents

E. W. HURST and M. STACEY. *British Journal of Experimental Pathology* [Brit. J. exp. Path.] 31, 410-442, June, 1950. 13 refs.

## BACTERIA

161. The Effect of Heparin on the Growth of Bacteria and Yeasts

J. R. WARREN and F. GRAHAM. *Journal of Bacteriology* [J. Bact.] 60, 171-174, Aug., 1950. 4 refs.

Experiments were designed to show the effect of heparin on the growth of *Micrococcus pyogenes* var. *aureus* and *Bacterium stewartii*. The medium in these experiments was a brain-heart infusion, and the heparin was in the form of the sodium salt. The pH of the heparin solution was 6.4. After 24 hours' incubation there were no significant differences in growth of organisms with concentrations of heparin ranging from 10 to 5,000 parts per million (p.p.m.).

In a protein-free medium, heparin was found to be bacteriostatic at concentrations of 100 p.p.m. or greater, but no bacterial effect was demonstrated at a concentration of 100,000 p.p.m. It is interesting to note that at this higher concentration a high percentage of mutants developed. Heparin failed to inhibit the budding of yeasts at a concentration of 10,000 p.p.m.

A. W. H. Foxell

**162. Comparison of a Liquid and a Solid Medium Method for Detection of Streptomycin-resistant *Mycobacterium tuberculosis***

S. BERNSTEIN, E. M. BRADLEY, E. M. MEDLAR, and W. STEENKEN. *American Review of Tuberculosis* [Amer. Rev. Tuberc.] **62**, 101-108, July, 1950. 11 refs.

The value of direct streptomycin-sensitivity testing on solid media was examined by comparing the results obtained on the Trudeau Society medium, containing 10, 50, and 500  $\mu$ g. of streptomycin per ml. before inspissation and assumed to contain 3, 5, 15, and 200  $\mu$ g. after inspissation, with those in the indirect sensitivity test on Dubos's "tween 80"-albumin liquid medium. The results obtained in 510 cultures are compared. There was close agreement between the results of the two tests when the bacterial population as a whole was either sensitive or resistant to streptomycin. With bacterial populations containing varying proportions of resistant and sensitive organisms, there was a 30% discrepancy between results in the two methods. In such cases use of the solid medium appears preferable because it indicates the relative proportions of sensitive and resistant organisms as well as the degree of resistance. A method of reporting results of sensitivity tests *in vitro* on solid media is presented.

E. Nassau

**163. Inhibition of Growth of Tubercle Bacilli by Certain Vitamin Analogues**

H. POPE and D. T. SMITH. *American Review of Tuberculosis* [Amer. Rev. Tuberc.] **62**, 34-47, July, 1950. 2 figs., 40 refs.

An earlier finding that tubercle bacilli grown on a simple synthetic nutrient medium are capable of synthesizing certain vitamins and vitamin analogues—namely, *p*-aminobenzoic acid, biotin, folic acid, inositol, nicotinic acid, pantothenic acid, pyridoxine, riboflavin, and aneurin—suggested the possibility that, should these compounds function in the micro-organism as essential metabolites, certain of their chemical analogues might be capable of acting as specific bacteriostatic agents. The degree of specificity of any inhibitory action caused by such an analogue could be investigated by testing the power of the related vitamin to counter its bacteriostatic action when both substances were included in the culture medium.

Two virulent strains of *Mycobacterium tuberculosis* were used, the human strain H37 Rv and the bovine strain Ravenel. In all, 96 compounds, 79 of them analogues of one or other of the above substances, were studied; their concentrations in the final media were varied from 1 to 100 mg. per 100 ml. The effectiveness of any compound to inhibit the growth of the micro-

organism was assessed from the macroscopic appearance and size of the surface pellicle formed on a modified Proskauer-Beck medium in horizontally-placed 4-ounce (114-ml.) medicine bottles incubated at 37° C. In a smaller series of experiments Dubos's liquid medium was used.

Of the compounds examined, 38 were found to inhibit the growth of the tubercle bacilli at concentrations below 100 mg. per 100 ml., but the activity of only 14 of these (10 analogues of *p*-aminobenzoic acid, 3 of biotin, and one related to guanine) was neutralized by the corresponding natural metabolite. The most active inhibitor of both strains of bacilli was 4-(imidazolidone-2) caproic acid, whose effect was completely neutralized by its related vitamin, biotin, 0.005 mg. per 100 ml., of the latter counteracting the effect of 0.5 mg. per 100 ml. of the former. A comparable, but less striking, reversible bacteriostatic effect was also observed with 5-amino-7-hydroxy-1-triazole-D-pyrimidine, a compound structurally related to the purine guanine. In view of the reversibility of this effect by the related natural metabolite and the ineffectiveness of other compounds as reversing agents, the activity of these substances as inhibitors of the growth of tubercle bacilli was regarded as specific and as attributable to some interference with either the synthesis or utilization of the natural metabolite by these micro-organisms.

G. Payling Wright

**164. The Nature of Tuberculin**

H. J. CORPER and M. L. COHN. *American Journal of Clinical Pathology* [Amer. J. clin. Path.] **20**, 603-609, July, 1950. 5 figs., 15 refs.

Tuberculin liberated by autolysis into liquid media during growth of tubercle bacilli at 37° C. can still be found in the medium without loss of biological activity after more than 8 years' storage in the incubator. Tuberculin solutions buffered to pH 7 without a preservative and sealed in amber glass ampoules remain stable for over 9 years at room temperature or in the refrigerator. Dilutions kept at 37° C. or in unbuffered saline are not stable. Heating the Seitz filtrate of 2-month-old cultures of human tubercle bacilli at or below pH 6 results in loss of tuberculin. This effect was less marked with an 8-year-old culture kept at 37° C.

E. Nassau

**165. Antibiotic Studies on Beta Hemolytic Streptococci: VII. Acquired *in vitro* Resistance to Bacitracin**

H. M. GEZON, D. M. FASAN, and G. R. COLLINS. *Proceedings of the Society for Experimental Biology and Medicine* [Proc. Soc. exp. Biol., N.Y.] **74**, 505-509, July, 1950. 10 refs.

Resistance to bacitracin was induced in  $\beta$ -haemolytic streptococci by 40 successive transfers on blood agar plates containing graded concentrations of the antibiotic; 23 strains of organisms of groups A, B, and C were used, and sensitivity to bacitracin was determined by the ditch-plate method. An increase in resistance varying from 8- to 3,750-fold was produced. Nine resistant strains became sensitive after 100 passages on bacitracin-free media, and also after 12 to 14 intracerebral passages in mice or storage at 4° C. for 20 months. The virulence for mice by intracerebral inoculation declined during the



production of resistance in 7 of 9 strains, a 10- to 10,000-fold increase in LD 50 occurring, but virulence was restored in 6 strains by further passage in mice. After the development of resistance the group-A and group-C strains still retained group specificity, but this was lost in 3 of 7 group-B strains; a conversion from alpha- to beta-haemolysis also occurred. The streptolysin-S titre was decreased in 2 of 3 resistant strains, but the development of resistance did not affect the ribose-nuclease or desoxyribose-nuclease activities of the organisms, or the proteinase-streptokinase ratio.

D. J. Bauer

166 (a). A Specific Serological Type of *Bact. coli* Found in Infants' Home in Absence of Epidemic Diarrhoea

A. M. M. PAYNE and G. T. COOK. *British Medical Journal* [Brit. med. J.] 2, 192-195, July 22, 1950. 8 refs.

166 (b). *Bact. coli* D 433 in Cases of Diarrhoea in Adults

J. S. STEVENSON. *British Medical Journal* [Brit. med. J.] 2, 195-196, July 22, 1950. 3 refs.

Both these articles are concerned with the aetiological relation between infantile gastro-enteritis and a particular strain of coliform organism variously known as *Bacterium coli* var *neapolitanum*, *Bact. coli*  $\alpha$  type, and *Bact. coli* D 433.

Payne and Cooke, investigating diarrhoea and vomiting in an infants' private residential home, recovered *Bact. coli* D 433 from rectal swabs of 2 infants suffering from gastro-enteritis. Because they also isolated the same organism from 2 other infant residents who were perfectly well and who were without any previous or subsequent history of gastro-enteritis, they decided to investigate further. The intestinal flora in relation to the clinical condition of all the residents was investigated by means of repeated rectal-swab examinations over a period of one year. Out of 60 infants under observation, *Bact. coli* D 433 was recovered on one or more occasions, often in pure culture, from 17 individuals. Eleven of these infants had no symptoms, one had a mild diarrhoea only, and 5 had infantile gastro-enteritis. There were 6 other babies in the period under review who had acute gastro-enteritis, but there was no D 433 strain in their stools.

In the second paper, the author discusses the recovery of *Bact. coli* D 433 from the stools of adults suffering from diarrhoea which did not appear to be due to an infective condition. Of a series of 72 patients examined during the early spring, 14 yielded cultures of D 433, but when a further 60 cases were examined in the autumn of the same year the organism was not encountered at all. During the examination of the first series the incidence of infantile gastro-enteritis was low, and certainly none of the series was in contact with such a case. The discussion centres round the possibility of the diarrhoea being responsible for the appearance of D 433 in the stools rather than the possibility that this organism was responsible for the diarrhoea.

[It is obvious from these papers and other recent reports on the subject that the aetiological relation between *Bact. coli* D 433 and infantile gastro-enteritis is by no means clear. Further laboratory, epidemiological, and clinical studies are indicated.]

H. J. Bensted

## IMMUNITY

167. A Rapid Method for Detection of Influenza Virus during Epidemics

S. S. KALTER. *Proceedings of the Society for Experimental Biology and Medicine* [Proc. Soc. exp. Biol., N.Y.] 74, 607-608, July, 1950. 1 ref.

During an epidemic of influenza, throat washings with nutrient broth were obtained from 28 patients. Quantities of 10 ml. were taken and from 2 to 4 ml. of a 1% suspension of chick or human type-O erythrocytes was added. The mixture was left at room temperature for 75 minutes, and the erythrocytes were then removed by centrifugation. The cells were resuspended in 0.8 ml. of saline and incubated at 37° C. for 2 to 4 hours, with occasional shaking. The tubes were then centrifuged. Any virus present in the original washing and adsorbed by the erythrocytes had now passed into the supernatant fluid and was detected by a simplified haemagglutination-inhibition test. An equal volume of a 1% erythrocyte suspension was added to part of the supernatant fluid, and to another part an equal volume of 1% erythrocyte suspension in a 1 in 50 dilution of antiserum to the PR8, Lee, or FM-1 strains of influenza virus; the result of the test was read after 30 and 75 minutes. The virus was detected and identified in 5 out of the 28 cases. While the method cannot be relied upon for the detection of virus in all cases where it is present, it is claimed by the author to be of value as a rapid preliminary method for the identification of the strain of virus prevalent in an epidemic.

D. J. Bauer

168 (a). Simultaneous Immunization of New-born Infants against Diphtheria, Tetanus, and Pertussis. Production of Antibodies and Duration of Antibody Levels in an Eastern Metropolitan Area

P. A. DI SANT'AGNESE. *American Journal of Public Health* [Amer. J. publ. Hlth] 40, 674-680, June, 1950. 2 figs., 8 refs.

A total of 199 full-term infants were inoculated with a triple vaccine containing *Haemophilus pertussis* ( $2 \times 10^8$  organisms per ml.) and tetanus and diphtheria toxoids adsorbed on aluminium hydroxide. Three doses were given, 0.5 ml. at the age of 1 week, 1.0 ml. at 5 weeks, and 1.0 ml. at 9 weeks. Some children also received a booster dose of 0.5 ml. between 6 months and 1 year of age. Before inoculation the blood of 98% of those infants tested contained no agglutinins to *H. pertussis*, but that of 15% contained appreciable amounts of tetanus antitoxin and that of 58% had "protective" titres (0.03 unit per ml. or more) of diphtheria antitoxin.

One month after inoculation the blood contained no pertussis agglutinins in 30% of cases, and in 54% titres regarded as sufficient to produce protection were found. A booster dose reduced the percentage of those without agglutinins to 16%. All the infants had more than 0.1 unit per ml. of tetanus antitoxin in the blood one month after inoculation and 85% had "protective" titres of diphtheria antitoxin. After a booster dose a "protective" titre of diphtheria antitoxin was found in all but one case, showing that active immunization

had been successful even in those previously immune at birth. When re-examined 9 months after immunization the blood of all the children still contained at least 0.1 unit per ml. of tetanus antitoxin, but the percentage of patients with "protective" titres of diphtheria antitoxin in the blood had fallen slightly and the percentage of children with "protective" levels of pertussis agglutinins in the blood had been halved. There was a more striking decrease in the number of children with high titres of each of the antibodies.

These results were compared with those obtained in a group of children who were similarly immunized after the age of 6 months. Although tetanus immunization was equally satisfactory in the two groups, higher titres of pertussis and diphtheria antibodies were obtained in the blood of the older children. It is suggested that the immunization of infants should be postponed to the third month of life.

D. G. ff. Edward

168 (b). **Simultaneous Immunization of Young Children against Diphtheria, Tetanus, and Pertussis. Experience in a Northern Metropolitan Area**

L. W. SAUER and W. H. TUCKER. *American Journal of Public Health* [Amer. J. publ. Hlth] 40, 681-685, June, 1950. 1 fig., 16 refs.

A small group of infants received 3-monthly inoculations of a combination of alum-precipitated diphtheria toxoid and *Haemophilus pertussis* vaccine, starting at the 4th month of life. Although 97% developed an adequate degree of protection against diphtheria, only 65% were adequately protected against pertussis.

Later two groups of infants were given a combination of *H. pertussis* vaccine and alum-precipitated diphtheria and tetanus toxoids, the injections being made deeply into each buttock alternately. The first group received three monthly inoculations beginning at the age of 6 months or later. The second group received four inoculations, at the 3rd, 4th, 5th, and 6th months of life respectively. When examined 3 months after the final inoculation all the 99 children in the first group were Schick-negative; 96% had a blood level of at least 0.1 unit of tetanus antitoxin per ml., and 83% had a satisfactory level of complement-fixing antibodies to *H. pertussis* in the blood. After a booster inoculation all the children developed adequate protection against pertussis. All 63 children in the second group became Schick-negative, and 96% had at least 0.2 unit of diphtheria antitoxin per ml. in the blood. The tetanus antitoxin titre was at least 0.1 unit per ml. in all cases, and in 98% there was an adequate level of pertussis-agglutinating antibodies in the blood.

D. G. ff. Edward

169. **Transmission of Staphylococcal Antitoxin (Anti-haemolysin) from Mother to Child**

J. MURRAY, R. M. CALMAN, and A. LEPINE. *Lancet* [Lancet] 2, 14-16, July 1, 1950. 2 figs., 10 refs.

The authors have estimated the serum staphylococcal antitoxin level, as indicated by its antihaemolytic effect on rabbit erythrocytes mixed with various dilutions of a standard staphylococcal toxin, in 56 mothers during labour, in the cord blood before expulsion of the placenta,

and in the peripheral blood of their infants within the first 24 hours of life. The antitoxin level of the cord blood was higher than the maternal level in 40 out of 54 cases, and that of the infants' blood higher than the maternal level in 42 out of 46 cases. In 31 cases the antitoxin level in the cord blood was over 50% higher, and in 18 of these over 100% higher, than that of the mother's blood. On average, the cord-blood antitoxin level was 63% higher than that of the mother. These findings are similar to those of Barr *et al.* (*Lancet*, 1949, 2, 324), who found the levels of diphtheria antitoxin higher in the cord blood than in the maternal blood.

A. Michael Davies

170. **Freeze-dried (Lyophilized) BCG**

F. VAN DEINSE and F. SENECHAL. *Tubercle* [Tubercle] 31, 157-163, July, 1950. 16 refs.

The authors describe the technique employed at the Pasteur Institute in Paris for freeze-drying B.C.G. vaccine. B.C.G. culture is suspended in 50% glucose solution and distributed into vials in quantities of 0.5 ml. The vials are placed in a hollow metal cylinder through which is passed a stream of paraffin oil cooled to  $-50^{\circ}\text{C}$ . This treatment causes freezing of the suspensions in a few minutes. The cylinder itself is then placed in an autoclave containing a methyl chloride spiral, which is maintained at  $-70^{\circ}\text{C}$ . A vacuum is created by means of a system of mercury diffusion pumps, and in the final stage phosphorus anhydride is introduced to remove the last traces of moisture. The end-product is a dry, spongy mass which can be reconstituted by adding 2 ml. of sterile water to the contents of the vial. A few seconds' shaking produces a homogeneous suspension with a strength of 75 mg. of B.C.G. per ml.

A series of experiments *in vitro* and *in vivo* were carried out in order to compare the viability and potency of the dried vaccine with those of preparations of equivalent strength which had not been subjected to the freeze-drying process. It was found that the number of colonies obtained on Löwenstein's medium inoculated with the freeze-dried suspension was not appreciably lower than with undried vaccine, but the colonies took a few days longer to develop. The vaccine retained full viability when the vials were stored in a refrigerator at  $+5^{\circ}\text{C}$ . for 3 months, and after 6 months only 10% of the bacilli were dead. The vaccine deteriorated more rapidly at room temperature. Guinea-pigs were inoculated intradermally and by scarification with fresh undried vaccine, with recently prepared dried vaccine, and with dried vaccine which had been stocked at room temperature for 2 to 3 months. The allergizing power of the undried and fresh dried vaccines, as judged by the strength of the reaction to tuberculin tests carried out 1 to 2 months after inoculation, was approximately equal, though the time taken for positive tuberculin reactions to develop was slightly greater in those animals inoculated with the dried vaccine. Storage of dried vaccine for more than 2 months at room temperature, however, caused some diminution in potency.

The protective effect of dried B.C.G. vaccine on guinea-pigs subsequently injected with virulent human tubercle bacilli was striking. Of 16 vaccinated guinea-pigs

killed and examined 5 months after infection, 4 were healthy and had no signs of disease, while the remainder showed only discrete tuberculous lesions 5 months after infection. All of 5 unvaccinated controls died spontaneously of tuberculosis or had advanced generalized disease at necropsy. The protection afforded by dried vaccine compared favourably with that afforded by fresh, undried B.C.G.

G. B. Forbes

#### 171. Serological Tests in the Diagnosis and Prognosis of Coccidioidomycosis

C. E. SMITH, M. T. SAITO, R. R. BEARD, R. M. KEPP, R. W. CLARK, and B. U. EDDIE. *American Journal of Hygiene* [Amer. J. Hyg.] 52, 1-21, July, 1950. 3 figs., 32 refs.

The technique of complement-fixation and precipitin tests for coccidioidomycosis is described, and the authors give a detailed account of their experience in the serological diagnosis of this disease, obtained from carrying out 21,000 tests in the last 10 years. Filtrates of cultures of *Coccidioides immitis* in asparagine synthetic medium, preserved with "merthiolate", were used as antigens. These are now marketed commercially in the U.S.A.

Serological tests were made after preliminary screening by skin tests, as it was found that in non-disseminated infections antibodies appeared only after skin sensitivity had developed. Antibodies appeared to be specific; they were not found in other infections, with the possible exception of severe cases of other mycotic diseases. Serological reactions were positive in more than 90% of hospital cases of coccidioidomycosis, but only in 7% of those with inapparent infections. In uncomplicated primary cases the complement-fixation (C.F.) test or the precipitin reaction, or both, might be positive. The C.F. reaction was more often positive in the more severe infections. The presence of precipitins was more often demonstrated early in the disease. The reactions were positive in 99% of patients in whom there were disseminated infections, 97% having a positive C.F. reaction.

Among the cases in which precipitins were at some time demonstrated, 90% gave positive reactions by the end of the second week; precipitins did not make their first appearance later than the fourth week. However, at that time in some cases previously positive the reaction had become negative, and at 5 months only 10% still gave a positive reaction. C.F. antibodies were slower in appearing; only in 20% was the reaction positive by 2 weeks and in some patients the antibodies did not appear for 3 months. By that time the antibodies in other patients had disappeared and it was rare for the C.F. reaction to be positive in uncomplicated infections after 6 months, although in a few patients it remained positive for years.

A positive precipitin reaction with a negative C.F. reaction was found in the less severe infections. The height of the titre in the C.F. reaction was to some extent proportional to the severity; titres of less than 1 in 32 suggested a good prognosis. Antibodies were demonstrated in only 40% of cases of pulmonary cavitation, and the titre in the C.F. reaction was usually low.

Only 2 patients with disseminated infections had negative reactions. Therefore in suspected cases negative reactions would be strong evidence against the diagnosis. In the cases of disseminated infection the precipitins tended to persist longer. The C.F. reaction titre was 1 in 32 or more in 56%; the height of the titre was to some extent proportional to the degree of dissemination. A fall in titre was a hopeful prognostic sign.

Antibodies were not found in the cerebrospinal fluid in the absence of meningitis.

D. G. ff. Edward

#### 172. The Effect of Adrenocorticotrophic Hormone on Circulating Antibody Levels

J. A. DE VRIES. *Journal of Immunology* [J. Immunol.] 65, 1-5, July, 1950. 17 refs.

A single dose of 50 mg. of an assayed adrenocorticotrophin preparation was injected intramuscularly into each of 8 rabbits effectively immunized against crystalline egg-albumen. Though all rabbits showed a sharp fall in the number of circulating lymphocytes within 4 hours of injection, no rabbit showed any sign of an increase in circulating antibody concentration up to 24 hours, while some showed a fall greater than might have been expected from the concomitant increase in plasma volume. The author suggests that lymphocytes may absorb and transport antibody, and that the administration of adrenocorticotrophin may lead not to their destruction, but to their concentration in tissues outside the circulation.

C. L. Oakley

#### 173 (a). Serological Relationships Existing between Bacterial Parasites and their Hosts. I. Antibodies in Human Blood Serum for Native Intestinal Bacteria

H. B. GILLESPIE, M. S. STEBER, E. N. SCOTT, and Y. S. CHRIST. *Journal of Immunology* [J. Immunol.] 65, 105-113, July, 1950. 22 refs.

Of 100 strains of bacteria (mostly coliform) isolated from the faeces of one healthy man, and 99 similar strains from the faeces of a second, many were agglutinated in significant titre by the serum of the men from whom they were isolated; the antibody titres remained fairly constant over 4 years. Ingestion of typhoid-paratyphoid vaccine led to a slight increase in the titre of agglutinins to several of their antigens in 2 of 3 volunteers. Ingestion by one volunteer of two killed coliform strains and of *Lactobacillus acidophilus* did not lead to the production of specific antibody.

C. L. Oakley

#### 173 (b). Serological Relationships Existing between Bacterial Parasites and their Hosts. II. The Agglutination of Intestinal Bacteria by Blood Serum from Human Beings and Animals not Known to Carry the Strains Tested

H. B. GILLESPIE, M. S. STEBER, and M. H. WAUGH. *Journal of Immunology* [J. Immunol.] 65, 115-118, July, 1950. 7 refs.

Specimens of serum obtained from a number of human beings were tested by agglutination against several of the coliform organisms referred to in the previous paper (Abstract 173 (a)); many gave positive results, often in surprisingly high titre.

C. L. Oakley



## Paediatrics

### 174. Absorption of Fat and Vitamin A in Premature Infants. I. Effect of Different Levels of Fat Intake on the Retention of Fat and Vitamin A

S. MORALES, A. W. CHUNG, J. M. LEWIS, A. MESSINA, and L. E. HOLT. *Pediatrics* [*Pediatrics*] 6, 86-92, July, 1950. 2 figs., 12 refs.

Eight healthy premature infants were studied in order to ascertain the retention of fat and excretion of vitamin A after administration of diets of high and low fat content. The ages of these infants were 11 to 28 days and their weights 1.3 to 1.8 kg. The experiment was divided into three periods, each of 4 days' duration. The fat intake was low (2%) in the first and third periods and high (6 to 8%) in the second period. The amount of fat retained during the first and third periods was 2.68 and 2.60 g. respectively, but during the second period this figure rose to an average of 9.22 g. per day.

The absorption of vitamin A varied considerably among the babies, but high-fat feeding had no deleterious effect on the absorption of this vitamin. This investigation shows that the percentage of the fat intake absorbed by the premature infant is the same whether it is given a high-fat or a low-fat diet. Thus increasing the amount of fat in the diet results in a correspondingly larger net absorption of fat. These infants took a high-fat diet without disturbance, and it is suggested that if further clinical trials confirm these results diets containing more fat than is generally prescribed might be advantageous for most premature infants.

Jas. M. Smellie

### 175. Physiologic and Chemical Response of Premature Infants to Oxygen-enriched Atmosphere

B. D. GRAHAM, H. S. REARDON, J. L. WILSON, M. U. TSAO, and M. L. BAUMANN. *Pediatrics* [*Pediatrics*] 6, 55-71, July, 1950. 14 figs., 23 refs.

This paper records the results of a study of the respiration and the oxygenation of arterial blood in 44 premature infants under normal atmospheric conditions and in an environment containing higher concentrations of oxygen. The infants ranged in age from 1 to 65 days and in weight from 1.1 kg. to 2.3 kg. Observations were first made while the infants were breathing atmospheric air, and then while the concentration of oxygen in the inspired air was cautiously increased. Blood samples were taken from the temporal artery, the methods and techniques used being described. The respiratory rhythm in the cases studied was of four types: (1) periodic with apnoea, (2) irregular with apnoea, (3) irregular with no apnoea, and (4) regular. In all those infants with breathing of types (1) and (2) in room atmosphere the rhythm became regular when oxygen was administered in a concentration of 75 to 90%, and in the case of type (3) when the oxygen concentration reached 50 to 75%.

In room atmosphere 27 infants had an average arterial oxygen saturation of 93%, which rose to 100% when

70 to 79% of oxygen was administered, and to an average of 102% in 80 to 89% oxygen. The average minute volume rose by 30% when 30 to 40% oxygen was administered, and the respiratory rate and total volume also showed an increase. It is concluded that the majority of premature infants under normal atmospheric conditions breathe as if suffering from oxygen lack, although their arterial oxygen saturation is not greatly reduced. Nevertheless, the administration of oxygen results in a normal type of breathing with increased pulmonary ventilation and a relative hyperpnoea.

Jas. M. Smellie

### 176. The Bacterial Content of Air in Children's Hospitals. Studies in the Children's Clinic and the Children's Castle of Helsinki. [In English]

A. HELVE. *Annales Medicinæ Experimentalis et Biologiae Fenniae* [*Ann. Med. exp. Biol. fenn.*] 28, Suppl. 6, 1-91, 1950. 13 figs., bibliography.

### 177. Discussion on Speech Defects in Children

H. MILLER, M. MORLEY, M. CRITCHLEY, E. M. CREAK, R. NOBLE, J. H. VAN THAL, E. STENGEL, and C. EDWARDS. *Proceedings of the Royal Society of Medicine* [*Proc. R. Soc. Med.*] 43, 579-588, Aug., 1950. 3 refs.

### 178. The Value of Breast-milk. (Was leistet die Frauenmilch?)

E. THOMAS. *Münchener Medizinische Wochenschrift* [*Münch. med. Wschr.*] 92, 445-446, June 23, 1950.

The reduction in the infant mortality from 20 or 30% at the turn of the last century to approximately 7% has been accredited to a great extent to the successful propaganda for breast-feeding. Thus it is not surprising that the decline in the incidence and duration of breast-feeding during the war years was followed by a new increase in the infant mortality to 20% and more. The need for a continuous campaign for breast-feeding, especially at critical times, becomes obvious.

Expressed breast milk is a useful substitute for breast-feeding, but it demands highly efficient methods of collection and bacterial control. Ready availability of expressed breast milk may also reinforce the propaganda for breast-feeding. Raw breast milk should be used immediately after expression, and the addition of lactic acid and streptomycin will reduce its bacterial content. Pooled breast milk should be boiled for 5 minutes and then chilled in the refrigerator for 5 hours before feeding. This procedure reduces the biological value of the milk and it becomes questionable whether its use in gastrointestinal disorders is superior to that of less expensive acidified cow's milk mixtures.

It is doubtful whether any increase in maternity benefits would be reflected in an increased rate of breast-feeding. It might be of more value to grant allowances to the mother for the first 3 months after delivery, particularly

in economically difficult times, as after a war. However, the mother's willingness to breast-feed should be stimulated primarily by giving her an increased sense of responsibility for the child's health. A higher standard of living and improvement of the health of the population as a whole will contribute decisively to the reduction of infant mortality.

M. Dynski-Klein

**179. Diastematomyelia (Congenital Clefts of the Spinal Cord). Diagnosis and Surgical Treatment**

D. D. MATSON, R. P. WOODS, J. B. CAMPBELL, and F. D. INGRAHAM. *Pediatrics* [Pediatrics] 6, 98-112, July, 1950. 10 figs., 9 refs.

The term diastematomyelia may be taken to include any abnormal cleft or division of the spinal cord or its intraspinal derivatives. This paper describes 11 cases in which an unusual type of occult spinal disorder was recognized and treated surgically in early childhood. The distinguishing feature of these cases was the projection of a discrete bony spicule from the posterior surface of a vertebral body through the spinal canal to transfix the spinal cord or cauda equina, usually in the midline. In most of these cases a visible cutaneous defect such as an abnormal tuft of hair, a skin dimple, a port-wine stain, or a cutaneous angioma overlay the neural abnormality. In the majority the presenting symptoms were associated with delay or difficulty in walking, and the true nature of the lesion was only revealed by careful radiological investigation of the spine. It is especially important to keep this developmental abnormality in mind when interpreting x-ray films which show spina bifida occulta. As the lesion does not cause any disturbance to the cerebrospinal-fluid circulation, lumbar puncture has no place in diagnosis.

The operative treatment of diastematomyelia consists in laminectomy with extradural removal of the bony spicule and division of all adhesions to the spina bifida occulta or cauda equina until the cord is freely movable within the dural canal. The early post-operative results have been encouraging, but only 2 patients have been followed up for more than 18 months. It is emphasized that in general little improvement can be expected from this operation, but the authors of this paper maintain that progression of the neurological disorder can be reduced, if not completely arrested.

Jas. M. Smellie

**180. Influenza in Infancy. Study of a Small Epidemic Identified by the Hirst Reaction. (La grippe du nourrisson. Étude d'une petite épidémie identifiée par la réaction de Hirst)**

R. A. MARQUÉZY and P. DEBRAY. *Semaine des Hôpitaux de Paris* [Sem. Hôp. Paris] 26, 2541-2548, July 14, 1950. 4 figs., 15 refs.

Clinical details are given of the 29 cases mentioned in a previous paper (see *Abstracts of World Medicine*, 1950, 8, 615) in which the serum gave positive evidence of recent infection with influenza A.

The first group, mild cases of upper respiratory tract infection often associated with otitis, gave serum antihaemagglutinin titres similar to those found in more severe cases. The second group was characterized by

fever, severe cough, cyanosis, and fine rales over both lung fields. Radiological examination revealed diffuse bilateral opacities, which usually persisted for 5 to 10 days but in exceptional cases were still present after 3 months. Otitis was a frequent complication. Treatment consisted of continuous administration of oxygen together with penicillin, sulphadiazine, and occasionally aureomycin. There were no deaths. In the third group (5 infants aged 3 to 16 months) onset was rapid, with diarrhoea and vomiting followed by acute fever and terminal convulsions. Radiographs of the chest were normal. In spite of antibiotic therapy 4 of these children died. [No results of bacteriological examinations are recorded. The direct bearing of influenza-virus infection on these cases is obscure since, as mentioned previously, many clinically indistinguishable cases without evidence of viral infection were admitted during the same period.]

J. F. McCrea

**181. Diagnosis and Treatment of Intracranial Haemorrhage in the Newborn by Subdural Puncture. (Diagnoza i leczenie krwawień śródczaszkowych noworodków metodą punkcji podoponowych)**

K. JERZYKOWSKA-KULESSZYNA. *Nowiny Lekarskie* [Now. lek.] 57, 110-111, June 1-15, 1950. 1 ref.

After a discussion of the aetiology and diagnosis of intracranial haemorrhage in the newborn, the method of subdural puncture used by Levine for differential diagnosis in these cases is described. A No. 20 spinal-puncture needle is pushed vertically through the coronal suture at the anterior fontanelle until it passes through the dura; this passage can be easily felt. Suction is made with a small syringe; if a subdural haematoma is present blood, fluid or partly clotted, or serum is obtained. Puncture was made in 31 suspected cases of intracranial haemorrhage at the University Clinic for Women, Poznań, between Aug., 1948, and Jan., 1950. Of these, 15 were cases of forceps delivery, 1 a case of breech delivery, 2 cases of Caesarean section, and 13 cases of spontaneous delivery. In 4 cases the result of puncture was negative; 3 of these infants were in good condition on leaving the clinic but 1 died from intrameningeal haemorrhage at the base of the skull, discovered on post-mortem examination. Of 27 infants with positive results on puncture, 8 subsequently died. Post-mortem examination (7 cases) revealed intracranial haemorrhage in 5 cases, and in 2 cases bronchopneumonia with oedema and congestion of the brain.

In 19 cases with positive results on puncture a great improvement in the condition of the infant occurred after the puncture, restlessness and convulsions ceasing. This encouraged the author to use this method as a therapeutic measure, and puncture was repeated at 1- or 2-day intervals until the result was negative. In 1 case only was there no improvement and after 6 punctures (all positive) the baby was taken home, where he soon died. When the rest of the babies were discharged from the clinic their condition was good, and in one very severe case follow-up for 8 months demonstrated that development was normal. The infants were also given vitamin K and oxygen and small transfusions of blood.

C. Uhma

## Medicine: General

182. **Physiology of Cold Bathing and its Accidents.** (Physiologie du bain froid et ses accidents) M. BOIGEY. *Presse Médicale* [Pr. méd.] **58**, 854-856, July 29, 1950. 8 refs.

The author describes the physiological changes which occur with cold bathing (at 0° to 24° C.). On entering cold water a sense of constriction is experienced in the chest, respiration becomes shallow and rapid, the pulse is small and rapid, and the skin blanches. This phase is soon followed by deeper breathing, easier movements, a warm sensation in the skin, which becomes bright red, and a full pulse. This feeling of well-being lasts from 10 to 15 minutes, and is followed by a cold sensation with stiffening of the muscles. When the bather leaves the water the skin feels warm but is insensitive for a time. If immersion is prolonged peripheral vasoconstriction is followed by vasodilatation and often by syncope. Certain persons with unstable vasomotor control, especially children under 16, experience severe cold, shivering, headache, and general muscle tightness. The skin has a sickly, pale, cyanotic appearance, similar to that in histamine shock. In people over 50 peripheral vasoconstriction may cause a reactive hypertension and cerebral haemorrhage. The author has seen 11 cases of hemiplegia beginning within an hour of cold bathing, and describes a case in a man of 61. He also suggests the following precautions. The period of cold bathing by untrained persons should not exceed 20 minutes, generalized reddening of the skin being a warning sign to leave the water. No bathing should take place for one hour after meals. Persons with respiratory infection, emphysema, or cardiac disease should not dive. The various theories of cold anaphylaxis, imperfect digestion, the trigeminal naso-pulmonary reflex, congestion, and cramp are discussed as aetiological factors. A test for cold anaphylaxis is described, susceptible people showing a papular eruption when ice or ethyl chloride spray is applied to the skin.

I. Ansell

183. **Clubbing of Digits, Metaplasia of Urinary Bladder and Mucous Diarrhea**

T. A. WARTHIN, J. F. COOPER, and A. P. CAPUTI. *Archives of Internal Medicine* [Arch. intern. Med.] **86**, 10-21, July, 1950. 5 figs., 7 refs.

Four male patients, aged 25 to 40 years, complained of extreme clubbing of fingers and toes (accompanied in 2 cases,\* and probably in a third, by hypertrophic osteo-arthritis), frequency of micturition (associated with striking metaplasia of the urinary bladder), and frequent passage of mucous stools and tenesmus. Two patients believed that clubbing had been present since adolescence, and one of these stated that his father's fingers had been similarly affected. In the other cases clubbing appeared suddenly 9 and 18 months before the onset of diarrhoea. Cystoscopy revealed the changes

of cystitis glandularis and cystica; large, irregular, apparently cystic masses were present, mainly in the trigonal and neck regions of the bladder; these consisted of mucosa and submucosa containing clumps of transitional epithelium, in some of which compound gland-like lumina had developed. The urine contained albumin and mucous threads and sometimes pus cells, but was sterile except immediately after cystoscopy or operative procedures. No other abnormalities were found except rectal tenderness and, in one patient, a raised erythrocyte sedimentation rate and slight hyperglobulinaemia. One patient has recovered almost completely, but the other 3 have shown little improvement after being ill for 6 to 7 years, although urinary symptoms were to some extent relieved by fulguration of the bladder and in one patient diarrhoea was controlled by "artane" (benzhexol). The authors do not know the cause of either the clubbing or the urinary-tract lesions. H. McC. Giles

184. **Stress and the General Adaptation Syndrome**

H. SELYE. *British Medical Journal* [Brit. med. J.] **1**, 1383-1392, June 17, 1950. 3 figs., 4 refs.

### ALLERGIC DISORDERS

185. **The Effect of Adrenocorticotrophic Hormone (ACTH) on Patients with Allergic Diseases—Facts and Speculations**

M. SAMTER. *Journal of Allergy* [J. Allergy] **21**, 296-302, July, 1950. 2 figs., 16 refs.

Six patients with bronchial asthma received either 0.8 mg. of adrenaline 4-hourly for 4 consecutive days or 50 mg. of adrenocorticotrophin 4-hourly for the same period. During the time of observation the excretion of 17-ketosteroids, 11-desoxycorticosteroids, and oxycorticosteroids was estimated. The results in one case are reproduced, and show a somewhat irregular parallelism between 11-oxycorticosteroid excretion and breathing reserve, both of which are sometimes high at the same period. It is also stated that attacks of bronchial asthma could be produced by prolonged administration of adrenaline. The author suggests that asthma might be produced either hormonally with participation of the cortex, the hypothalamus, the anterior pituitary gland, and the adrenal cortex, by upset of the vagus-sympathetic equilibrium, or by local histamine release.

[The facts given are scanty and their basis is uncertain. The breathing reserve is based on a hyperventilation test which, in asthmatics, is unreliable because hyperventilation in asthmatics causes a very variable increase in bronchial spasm; the assumed normal range of excretion of 11-oxycorticosteroids is called arbitrary by the author himself, but the experimental basis of this range is not given. The speculations bear little relation to the facts.]

H. Herxheimer



**186. The Effect of Pituitary Adrenocorticotrophic Hormone (ACTH) on Histamine Intoxication and Anaphylaxis in the Guinea Pig**

S. FRIEDLAENDER and A. S. FRIEDLAENDER. *Journal of Allergy* [J. Allergy] **21**, 303-309, 1950. 32 refs.

Guinea-pigs were exposed to histamine aerosol in a chamber, and the time elapsing before they showed the first signs of coughing or choking was measured. When amounts of 1.64 to 4.1 mg. of adrenocorticotrophin (ACTH) had been injected 2, 4, or 6 hours beforehand, the animals reacted to histamine aerosol in much the same way as those not given ACTH. In another series of experiments guinea-pigs were sensitized by intraperitoneal injection of 0.1 ml. of horse serum. When, 14 to 18 days later, a shock dose was administered intravenously, ACTH given in the same dosage as in the first series failed to protect the animals, whether the shock induced was fatal, severe, or mild.

H. Herxheimer

**187. The Effect of Cortisone upon the Release of Histamine during *in vitro* Hemolytic Reactions in Rabbit Blood**

H. M. CARRYER and C. F. CODE. *Journal of Allergy* [J. Allergy] **21**, 310-313, July, 1950. 10 refs.

Rabbits were sensitized to washed sheep erythrocytes, and sheep erythrocytes with and without cortisone were then added to samples of their blood. The release of histamine in the ensuing haemolytic reaction was not altered by the presence of 10 to 50  $\mu$ g. of cortisone per ml. of blood, even if the blood was incubated with cortisone one hour before the addition of the sheep cells.

H. Herxheimer

**188. The Effect of Cortisone on Bronchial Asthma and Hay Fever occurring in Subjects Sensitive to Ragweed Pollen**

H. M. CARRYER, G. A. KOELSCH, L. E. PRICKMAN, C. K. MAYTUM, C. F. LAKE, and H. L. WILLIAMS. *Journal of Allergy* [J. Allergy] **21**, 282-287, July, 1950. 3 figs., 16 refs.

Three patients suffering from asthma and rhinitis due to sensitivity to ragweed pollen were given either 100 mg. cortisone acetate or 100 mg. cholesterol intramuscularly daily over a period of 4 weeks; each substance was given at least for 6 consecutive days. Cortisone brought relief from asthma within one day, while the hay-fever symptoms decreased within 2 or 3 days. When cortisone was discontinued the allergic symptoms returned after about 3 days.

H. Herxheimer

**189. Pollen Tolerance Nasal Tests in Hay Fever. Experimental and Clinical Observations**

L. TUFT and G. I. BLUMSTEIN. *Journal of Allergy* [J. Allergy] **21**, 326-333, July, 1950. 4 figs., 2 refs.

The pollen content of the blunt end of a toothpick was examined by blowing the pollen from the toothpick on to a petrolatum-covered surface and counting the granules deposited. Three counts of ragweed pollen showed about 18,000 granules, with a deviation of 2.6%. The pollen was diluted with talcum and different concentrations

(from 1 in 1,000 to 1 in 1) inhaled through one nostril. The induction of sneezing together with rhinorrhoea and blockage was considered a positive result.

Forty-four patients were thus tested before pre-seasonal hay-fever treatment was started and again after the end of the pollen season. Of these, 25 showed an increased tolerance, 14 showed no change, and 5 a decrease. Most of the patients, even those with decreased tolerance, reported good results from the treatment received. When 21 patients receiving perennial treatment over a period of 3 to 6 years were tested their tolerance was seen to increase year by year. (The representative graphs of 2 patients are reproduced.) Patients with very variable results had bouts of symptoms under the influence not only of pollen, but also of respiratory infections, meteorological factors, and psychological stimuli. If a spontaneous remission or cure occurred, the reactions became negative, and the test is therefore useful for deciding whether further specific therapy is necessary.

H. Herxheimer

**190. The Incidence of Abnormal Electroencephalographic Patterns in Allergic Children**

R. CHOBOT, H. D. DUNDY, and B. L. PACELLA. *Journal of Allergy* [J. Allergy] **21**, 334-338, July, 1950. 4 refs.

Eighty children, mostly between 5 and 14 years old, and suffering from asthma, eczema, or allergic rhinitis, were investigated by electroencephalography. One-third had abnormal electroencephalographic patterns. Slow potentials were regarded as abnormal if they were encountered more frequently than in normal children. In 42 relatives of abnormal children 38% of electroencephalograms were also abnormal. "Trimeton", an antihistamine drug, given in three daily doses of 25 mg., failed to alter the abnormal patterns in these children.

H. Herxheimer

**191. Bronchiectasis in Asthma**

G. L. WALDBOTT, J. M. KAUFMAN, and K. J. MERKLE. *Journal of Allergy* [J. Allergy] **21**, 339-343, July, 1950. 4 figs., 4 refs.

In 28 cases of bronchial asthma in which haemoptysis, purulent expectoration, or persistent rales were present, bronchograms were taken. Only in 4 of them was evidence of saccular or cylindrical bronchiectasis found; in 15 there was no evidence at all, and in 9 there was some widening of secondary bronchi in some part of the lung, with absence of foliage. Radiologists were not in agreement on the point whether these changes should be termed bronchiectasis; in some cases they were not found after an interval of several months and they are therefore regarded as reversible. The term pseudo-bronchiectasis is suggested for them.

H. Herxheimer

**192. Has "Vigantol" [Calciferol] an Anti-allergic Action? (Wirkt Vigantol antiallergisch?)**

— WEICKSEL. *Zeitschrift für Tuberkulose* [Z. Tuberk.] **95**, 141-146, 1950. 27 refs.

The author found, in accordance with experiments in animals, that both attacks of typhoid fever and typhoid vaccination have a favourable influence on

the course of tuberculosis. Heterologous antigens, such as typhoid antigen or *Bacterium coli* vaccine, may stimulate the production of specific antibodies against tuberculosis. This means that specific allergy can be enhanced by non-specific allergens (hetero-allergy). A parallelism is therefore assumed between hetero-allergy and the specific tuberculous allergy. The typhoid agglutination titre in the blood of patients who have either successfully overcome a typhoid infection or been vaccinated against typhoid is considered to reflect the patient's allergic state. The typhoid agglutination titre in such cases could regularly be reduced by treatment with small doses of "vigantol" (vitamin D<sub>2</sub>), from 0.5 to 1 mg. (20,000 to 40,000 i.u.) a day. From these findings, and a fall in erythrocyte sedimentation rate and slight rise in lymphocyte count after 4 weeks of vitamin D<sub>2</sub> treatment, the author concludes that small doses of the vitamin have an anti-allergic action and a beneficial effect on pulmonary tuberculosis.

E. G. W. Hoffstaedt

## METABOLIC DISORDERS

### 193. Hypervitaminosis D in Infancy. (Die D-Hypervitaminose im Säuglingsalter)

G. FANCONI and E. DE CHASTONAY. *Helvetica Paediatrica Acta* [*Helv. paediat. Acta*] 5, Suppl., 5-36, July, 1950. 14 figs., 33 refs.

The authors report 4 cases of hypervitaminosis D<sub>2</sub>, 3 in babies and one in an older child. They were taken ill as a result of the administration of excessive amounts of vitamin D<sub>2</sub>. The symptoms were on the whole the same and consisted of loss of weight, cessation of growth, vomiting, intense constipation, polydipsia, and polyuria. The blood pressure and the erythrocyte sedimentation rate were raised. The calcium level in the blood was high. The phosphorus level varied; in 3 cases it was low and in the fourth case increased. The amount of serum phosphatase was low while the concentration of non-protein nitrogen was raised. The erythrocyte and leucocyte counts were normal but there was an increase in eosinophil count. Radiographs revealed calcification of the epiphyses and marked osteolysis in the region of the metaphysis. According to the authors children with hypothyroidism are more liable to be affected by this hypervitaminosis than are children with rickets. They recommend the Sulkowitch reaction as a means of early diagnosis of hypervitaminosis.

Franz Heimann

### 194. Blood Pyruvate Levels following Intravenous Glucose Injections in Aged Males

L. E. SMITH. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] 220, 78-83, July, 1950. 2 figs., 15 refs.

The author studied the pyruvate levels in arterial blood after the intravenous injection of 50 ml. of 50% glucose solution into three groups of elderly males: (1) 13 patients (age range 45 to 84; mean 61 years) with normal glucose tolerance; (2) 10 patients (age range 44 to 83; mean 67.4 years) with blood glucose curves

which had not returned to the fasting level within 2 hours of intravenous injection of glucose; (3) 7 patients with diabetes mellitus (age range 57 to 83; mean 68.3 years) who had been without insulin for 72 hours.

The mean fasting levels of pyruvate in the blood for the three groups were 1.28, 1.44, and 1.50 mg. per 100 ml. respectively, and the maximum mean pyruvate values obtained 30 to 50 minutes after injection were, respectively, 1.76 and 1.91 mg. in the two non-diabetic groups and 1.62 mg. per 100 ml. in the diabetic group. The latter rise is not significant, but the difference between the rise observed in the two non-diabetic and the diabetic groups is statistically significant. The arterial pyruvate level was always higher than the venous level in the one case studied.

In depancreatized dogs or diabetic patients there is no rise in blood pyruvate level after glucose injection unless insulin is administered; therefore the author concludes that insulin deficiency is not the primary factor responsible for the prolonged rise in glucose level in tolerance tests on aged subjects, since the maximum mean rise in blood pyruvate level in the two non-diabetic groups was not significantly different.

R. P. Hullin

### 195. The Syndrome of Malignant Malnutrition. Observations on the Relation of the Serum Proteins to the Occurrence of Oedema and the Effect of Diet

E. JANSSEN and J. S. LE ROUX. *South African Journal of Clinical Science* [*S. Afr. J. clin. Sci.*] 1, 100-113, June, 1950. 52 refs.

A series of 101 children with malignant malnutrition (infantile pellagra, kwashiorkor) in Pretoria were studied to ascertain the relation between oedema, serum protein level, and diet in this condition. On admission, pitting oedema was present in all cases and skin lesions in most. Serum protein and albumin were estimated by the nesslerization method of King. The cases were divided into two groups, the first group consisting of 50 patients who received a diet containing skimmed milk, vegetables, minced meat and minced raw liver, and injections of liver extract and vitamins. The second group of 51 patients received during the first 4 to 7 days specially prepared casein-supplemented skimmed milk before being put on the treatment given to the first group. On this treatment 18 patients in the first group and 13 patients in the second group died.

The serum protein levels on admission, determined in 18 patients in the first group and in 23 in the second, were below normal; this was especially true of the albumin levels. It is stated that the degree of oedema could not always be correlated with the serum protein level. With treatment there was a rise in the serum protein level, accompanied by subsidence of oedema; in those who recovered, the oedema disappeared completely after 8 to 12 days in the second group, and after 10 to 19 days in the first group. No critical serum protein level could be established at which oedema either appeared or disappeared. The presence of small amounts of albumin in the urine in a large number of cases led the authors to think that renal changes possibly play a part in the production of the oedema. It was thought that hypoproteinaemia was not the only factor, and from a

consideration of the literature the authors believe that other factors, such as tissue pressure, capillary permeability, and hypertrophy of the adrenal glands, may be involved in the pathogenesis of the oedema of malignant malnutrition.

[More information, instead of much theoretical discussion, should have been given concerning the serum protein levels before and during treatment, the age and sex distribution of the cases, the dietary history, and the incidence of protozoal and helminthic infections.]

H. M. Sinclair

**196. Neurological Manifestations of Acute Porphyria.** (Les manifestations neurologiques de la porphyrie aiguë)

M. BONDUELLE, J. SIGWALD, —. DEBUIRE, and —. PIOT. *Revue Neurologique* [Rev. neurol.] 82, 233–244, April, 1950. 1 fig.

This is an account of the detailed clinical examination of 2 patients with acute porphyria and of the family of the second patient, in which some members of the second and third generations were found to have symptoms suggesting porphyria, together with porphobilinogen and porphyrins in the urine. The first patient was seen in June, 1949, with a rapidly progressive polyneuritis of unknown aetiology. The illness had begun in February with abdominal pain which was thought to be due to cholecystitis. After this, severe pains in the legs developed, followed by paralysis of the legs and arms. By the middle of March a flaccid quadriplegia with retention of urine and faeces existed. Some regression of the paralysis took place at the beginning of June, but it soon recurred and was accompanied by amyotrophy of the arms and legs. At the end of July the condition of the patient became worse, with pyrexia, severe, colicky, abdominal pains, and meningeal irritation, but there was no pleocytosis in the cerebrospinal fluid. Porphyrins were found in the urine. The mild meningism persisted until August 16, when the patient died (presumably from respiratory paralysis), the flaccid quadriplegia having remained unchanged. Necropsy was not performed.

The second patient, a woman aged 40, was seen in October, 1949, with a severe polyneuritis accompanied by psychological symptoms, the clinical picture suggesting an alcoholic polyneuritis. The paralysis was predominant in the legs and was accompanied by a symmetrical amyotrophy. Porphyrinuria was present, but not in sufficient amount to discolour the urine. The patient had had frequent attacks of severe abdominal pain and vomiting since adolescence, and also frequent headaches and psychological disturbances—confusion and hallucinations. After 2 months in hospital the patient was able to walk again.

The various neurological manifestations of acute porphyria are discussed. Serious psychological symptoms are particularly frequent—Waldenström noted them twenty times in his review of 100 cases—and may consist of disorders of memory, depression, agitation, hallucinations, or violent delirium, often associated with abdominal symptoms and other neurological symptoms. All the symptoms and signs tend to be

paroxysmal and variable. Polyneuritis is one of the most frequent neurological manifestations. This may at first be confined to one limb and may develop into a flaccid quadriplegia with amyotrophy. Slow regression of the paralysis may take place. An almost constant feature of the polyneuritis is the absence of any sensory disturbance. Meningeal irritation may occur, but it is not accompanied by an increase in the cerebrospinal-fluid pressure or any great increase in the cell or protein content of the fluid.

The authors emphasize that the port-wine colour of the urine, which is usually regarded as the most decisive clinical sign of porphyria, may be absent throughout the evolution of the disease, but porphobilinogen may be converted into the coloured porphyrins by acidification of the urine and boiling for 10 minutes. The familial aspects of the disease are discussed and it is pointed out that although it may be inherited as a dominant trait, its manifestations may remain latent.

J. MacD. Holmes

**197. Effects of Adrenocorticotrophic Hormone (ACTH) in Gout**

A. B. GUTMAN and T. F. YÜ. *American Journal of Medicine* [Amer. J. Med.] 9, 24–30, July, 1950. 1 fig., 16 refs.

A series of 11 cases of acute gout were treated with adrenocorticotrophin (ACTH). Seven, including one refractory to colchicine, responded well, though in some cases the response was not superior to that obtained with colchicine, and in 4 patients with an unsatisfactory response to ACTH the attack was rapidly terminated by colchicine. Cessation of ACTH therapy was followed in 4 cases by relapse. ACTH is not suitable for prophylactic treatment. The view is expressed that the benefits of ACTH in acute gout are unrelated to a specific uricolytic action and that the available evidence does not incriminate the pituitary-adrenal mechanism as having any specific pathogenic role in gout. Henry Cohen

## DIABETES

**198. A Study of Atherosclerosis in a Group of Diabetic Patients**

J. I. GOODMAN, S. WASSERMAN, L. J. MARCUS, and L. FRANKEL. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 220, 30–45, July, 1950. 5 figs., 40 refs.

At Mount Sinai Hospital 79 out of 89 diabetic patients were found to be suffering from atherosclerosis. Most of the patients were more than 50 years of age. Various methods were employed in order to establish the presence of atherosclerosis in the aorta and other large blood vessels. In 83 cases percussion tests and radiological examination of the chest indicated that the aortic arch was enlarged. The enlargement was attributed to senescence rather than to diabetes mellitus. Calcification of the thoracic aorta, an important sign of atherosclerosis, was detected in 37 cases and a positive carotid-sinus reaction was elicited in 61 cases. A study of the electrocardiographic findings showed that the carotid-sinus



reaction constituted a sensitive index of the presence of atherosclerosis in the coronary arteries. In 51 cases there was abnormal pulsation in the supraclavicular region, and 44 patients had an accentuated aortic second sound. Little reliance was placed upon variations in the blood pressure in assessing atherosclerosis. In 51 cases calcified intimal plaques were discerned on radiological examination of the abdominal aorta. Although calcification of the pelvic and femoral arteries was found in about 50 cases it was not possible to differentiate atherosclerosis from medial sclerosis. In 41 patients clinical examination revealed occlusive phenomena due to disease of the arteries of the lower limbs. A diagnosis of retinal arteriosclerosis was made in 39 instances, but little correlation was established between this finding and the presence of atherosclerosis in the peripheral arteries.

Basing their opinion on the pathological findings in 5 amputated gangrenous legs, the investigators consider that occlusive changes in vascular disease of the legs are due to fibrosis and not to thrombosis. Atheroma affects the arteries of the thigh; fibrosis occurs in the arteries of the leg.

A. Garland

199. **Diabetes and Hepatitis.** (Diabetes und Hepatitis) M. OPPENHEIM. *Gastroenterologia [Gastroenterologia, Basel]* 75, 273-320, 1950. 14 figs., bibliography.

An analysis of the interplay between diabetes and infective hepatitis was carried out in 46 cases in which the two diseases occurred together, 200 cases of uncomplicated infective hepatitis being used as controls.

Of the patients in whom both diseases were present, 30 were women and only 16 men. No such sex difference exists when either of the diseases occurs alone. Whereas the incidence of uncomplicated hepatitis appears related to the age of the patient, reaching its peak during the third decade, the incidence of hepatitis combined with diabetes is determined neither by the age of the patient nor by the duration of the diabetes, but by its severity.

In the diabetic patient the symptoms of hepatitis come on more slowly and take longer to subside. Contrary to what might be expected, the fleeting hepato-renal syndrome which frequently occurs during the first few days after the onset of jaundice does not precipitate any of the more serious renal complications of diabetes; the concomitant diabetes even tends to suppress the renal component of infective hepatitis. Lipaemia, which is a feature of both diseases, becomes more pronounced if they occur together. The total cholesterol content of serum tends to be higher than for hepatitis alone, and the value for the esterified fraction lower. The fall in the ester level comes on and recedes more slowly than in the uncomplicated cases.

The haematological changes of hepatitis may also be observed when it is complicated by diabetes, but they are less marked and also follow a more protracted course. The incidence of the fleeting positive Wassermann reaction, which is a frequent feature in uncomplicated cases of hepatitis, is reduced by half when the two diseases occur together. A definite correlation between the serum-iron and serum-bilirubin curves was found

in most cases of uncomplicated hepatitis. This correlation was completely upset in diabetes.

The effect of hepatitis on diabetic metabolism is already apparent in the incubation period. It usually leads to an initial improvement in the diabetes, consisting in a considerable increase in carbohydrate tolerance, which is attributed to a stimulation by the diseased liver of the remnants of functioning islet tissue. Ketone bodies usually disappear, a phenomenon perhaps due to the inability of the diseased liver to produce them. The initial improvement generally changes later on to deterioration.

Although the author believes that diabetic patients are genuinely more susceptible to infective hepatitis, quite apart from any increased exposure due to syringe infection, he was unable to discover the cause of this in his analysis of the combined diseases.

R. Schneider

## 200. **Studies on Diabetic Rats: the Production of Cardiovascular and Renal Disease in Diabetic Rats**

J. M. R. BEVERIDGE and S. E. JOHNSON. *British Journal of Experimental Pathology [Brit. J. exp. Path.]* 31, 285-293, June, 1950. 12 figs., 21 refs.

Rats weighing about 200 g. were made diabetic by subcutaneous injection of 185 mg. of alloxan per kg. of body weight. Basal diet was fed to 24 normal control rats (group I), and to 24 diabetic rats (group II). Group III had a diet containing 70% fat, and group IV had this diet except that 0.5% cholesterol was added at the expense of starch. Group V received a basal diet in which 0.5% of starch had been replaced by 0.5% cholesterol. All the animals except those in group I were diabetic. They were given protamine zinc insulin from time to time according to their condition, but no attempt was made to control their diabetes.

After 7 to 11 months a number in each group were killed. The remaining animals were permitted to live their life span, average survival in group II being 268 days, in group III 217 days, in group V 203 days, and in group IV 151 days. Tissue was fixed in 10% formalin and stained with haematoxylin and eosin, and Weigert's elastic stain for vascular lesions. Aortas were split and stained with Sudan IV.

In sections of the myocardium there was evidence of myocarditis in all the groups except group I. Vessels, including those of heart, kidney, and pancreas and the aorta, showed no significant intimal lesion. Pyelonephritis was present in almost 100% of diabetic animals and 63% of those in group I. The microscopic lesions included chronic pyelitis, dilatation of tubules with increase of interstitial tissue, and hyalinization of the glomeruli.

A control group of 15 rats were given an injection of alloxan and killed at intervals up to 14 days. Myocardial lesions were found up to 7 days only, and renal tubular lesions up to 14 days.

Peter Harvey

## 201. **Studies on Diabetic Rats: the Effect of Diabetes and of Diet upon the Plasma and Liver Lipids of Rats**

J. M. R. BEVERIDGE and S. E. JOHNSON. *British Journal of Experimental Pathology [Brit. J. exp. Path.]* 31, 294-305, June, 1950. 7 figs., 26 refs.

# Cardiovascular Disorders

## HEART

### 202. A Phonocardiographic Study of Apical Diastolic Murmurs Simulating those of Mitral Stenosis

A. A. LUISADO and L. P. MONTES. *Annals of Internal Medicine* [Ann. intern. Med.] 33, 56-72, July, 1950. 12 figs., 17 refs.

The phonocardiogram can be made to reveal some very disconcerting inaccuracies in our conventional assessment of apical diastolic murmurs. Many such murmurs mimic that of mitral stenosis, yet may be caused by such diverse lesions as adherent pericardium, hyperthyroidism, left ventricular enlargement, aortic insufficiency, coronary or hypertensive heart disease, or mitral insufficiency without appreciable stenosis. Some apparently apical diastolic murmurs are in fact auscultatory illusions, caused either by a gallop rhythm or by a crescendo type of first sound. Similar illusions may arise from a split second sound in bundle-branch block or from a systolic snap from traction upon established adhesions.

Apart from clear and obvious mitral stenosis, a rumbling apical diastolic murmur may be associated with aortic insufficiency, as in the Austin-Flint murmur, or it may be due to the rapid passage of blood from a large left auricle through a normal mitral orifice into a relatively still larger left ventricle.

[This article is yet another warning, if such be still needed among students and teachers, to beware of the "presystolic habit".]

G. F. Walker

### 203. The Electrocardiogram in Chronic Constrictive Pericarditis. (L'électrocardiogramme de la péricardite constrictive chronique)

P. SOULIÉ, G. VOCI, and J. NICHYANPOULOS. *Archives des Maladies du Cœur et des Vaisseaux* [Arch. Mal. Cœur] 43, 635-648, July, 1950. 3 figs., bibliography.

The authors discuss the electrocardiographic findings in chronic constrictive pericarditis and report the findings in 7 cases. Only standard and V leads were taken. In cases with sinus rhythm the changes in the P wave are the most constant and important, besides the well-known alterations in the QRS wave, ST segment, and T wave. The characteristics of the P wave are: increased duration (beyond 0.10 second), high voltage, and bifid shape; in leads V1 and V2 it is diphasic; the axis lies between 0 and 75 degrees. The authors note that this P wave is quite different from the "pulmonary" P (attributable to right auricular hypertrophy), but may simulate the "mitral" P, as happened in one of the 7 cases. It is believed that the determining factors in the appearance of the "constrictive" P wave are mechanical and inflammatory. Less characteristic were the changes in the ST segment and T wave. The ST segment was

either isoelectric or, more frequently, deflected downwards in 2 or 3 peripheral leads. This was usually noticeable either in L2, L3, and VF, or in L1 and L2. The T wave was, in typical cases, low or inverted in all leads. However, in some patients the T wave may be isoelectric, diphasic, or inverted in one or more leads. Exceptionally the T wave remains normal. No difficulty should arise in its differentiation from the "coronary" T. The voltage of QRS was low, but this was not a constant finding. For example, in one of these cases QRS was perfectly normal in all leads. In conclusion, the alterations in the P wave are first in importance, and their discovery is a great help in diagnosis. The abnormal pattern may disappear after pericardiectomy.

A. I. Suchett-Kaye

### 204. The Electrocardiogram in Congenital Heart Disease. (A Postmortem Correlation Study of 53 Cases)

M. H. UHLEY. *Annals of Internal Medicine* [Ann. intern. Med.] 33, 188-210, July, 1950. 8 figs., 23 refs.

The author has attempted to re-evaluate the electrocardiographic findings in congenital heart disease on a basis of 53 cases that came to necropsy at the Michael Reese Hospital, Chicago, between the years 1920 and 1948. In the majority (31), only limb-lead electrocardiograms were taken. The series included 15 cases of calcific aortic-valve disease, alleged to be secondary to congenital bicuspid aortic valve. Of the remaining 38 there were 7 with atrial septal defect (or patent foramen ovale), 3 with coarctation of the aorta, 3 with patent ductus, 3 with ventricular septal defect, and 2 with "defect of the pulmonary conus or artery", a total of 18 instances of the six common types of congenital heart disease.

Paul Wood

### 205. Unipolar Electrocardiography in Congenital Heart Anomalies. (Unipolare Elektrokardiographie kongenitaler Anomalien des Herzens)

W. WEISSEL. *Cardiologia* [Cardiologia, Basel] 16, 191-231, 1950. 7 figs., bibliography.

### 206. Intracardiac and Intravascular Potentials resulting from Electrical Activity of the Normal Human Heart

C. E. KOSSMANN, A. R. BERGER, B. RADER, J. BRUMLIK, S. A. BRILLER, and J. H. DONNELLY. *Circulation* [Circulation] 2, 10-30, July, 1950. 10 figs., 42 refs.

### 207. Pulmonary Hypertension in Heart Disease

C. W. BORDEN, R. V. EBERT, R. H. WILSON, and H. S. WELLS. *New England Journal of Medicine* [New Engl. J. Med.] 242, 529-534, April 6, 1950. 5 figs., 23 refs.

The pressure in the pulmonary artery was measured directly by cardiac catheterization in 30 patients with mitral stenosis and one with mitral incompetence, in varying stages of heart failure, and in 23 patients with

left ventricular failure at the U.S. Veterans Administration Hospital, Minneapolis, Minnesota. In the group with mitral disease the pressure in the pulmonary artery was consistently raised and the degree of hypertension could be correlated with the functional capacity of the heart; the severest degree of pulmonary hypertension was recorded in the advanced cases of mitral stenosis. It was also shown that the most important clinical manifestations of mitral stenosis could be explained on the basis of pulmonary hypertension, and that such physical signs as accentuation of the pulmonary second sound, the Graham-Steell murmur, enlargement of the right heart, and dilatation of the pulmonary artery were entirely dependent on the existence of a high pulmonary arterial pressure. In the patients with left ventricular failure no constant correlation between pulmonary hypertension and functional status of the heart was found and the reduction in vital capacity was not proportional to the rise in pulmonary arterial pressure. Among the factors producing this pulmonary hypertension, increase in pressure in the pulmonary vein and an increased resistance to the pulmonary blood flow were shown to be the most important.

A. I. Suchett-Kaye

208. **Coronary Phlebothrombosis and Thrombophlebitis. Part II. Experimental (Flebotrombosis y tromboflebitis coronaria. II. Parte experimental)**  
R. ZUCKERMANN, A. BISTENI, J. ORTIZ, and D. SODI PALLARES. *Archivos del Instituto de Cardiología de México* [Arch. Inst. cardiol. Méx.] 20, 286-296, June 30, 1950. 5 figs., 2 refs.

The injection of cultures of hemolytic streptococcus or of *Staphylococcus aureus* directly into the pericardial sac of dogs produces thrombosis of the coronary veins and electrocardiographic changes suggestive of pericarditis, although there are no histological changes suggestive of superficial myocarditis. The changes of RS-T and T observed in purulent pericarditis are attributed to the consecutive coronary thrombophlebitis. —[Authors' summary.]

209. **Cardiac Disease and Rheumatoid Arthritis**

- J. Y. BRADFIELD and M. R. HEJTMANCIK. *Archives of Internal Medicine* [Arch. intern. Med.] 86, 1-9, July, 1950. 22 refs.

An analysis was made of the case records of 154 patients investigated in the south-west of the United States. It was decided to select 45 case records of patients aged less than 50 years and suffering from uncomplicated rheumatoid arthritis. A past history of rheumatic fever was not elicited in any of these cases. Although evidence of active disease was found in the majority of the patients, the illness was considered to be acute in only 7 instances. Sixteen patients had some form of cardiac disturbance. The series included 7 patients with clinical, radiological, and electrocardiographic evidence of organic heart disease, but with few symptoms pointing to the presence of a cardiac abnormality. One of these patients was a woman, aged 32 years, who had suffered from rheumatoid arthritis for a period of 6 months. A

soft systolic murmur was detected at the apex of the heart. A skiagram of the chest revealed slight cardiac enlargement and a prominent conus. On electrocardiographic examination the T waves were observed to be abnormal in all leads. The authors also collected data on a group of 6 arthritic patients with cardiac disease and a history of rheumatic fever. These patients were considered to be suffering from a disease which typified the transition from rheumatic fever to rheumatoid arthritis.

It appears that clinical evidence of organic heart disease is present in 10% of cases of rheumatoid arthritis. At necropsy on patients with this disease cardiac abnormalities are found to occur in ratios ranging from 1:3 to 1:2. The possibility exists that rheumatic fever and rheumatoid arthritis are allergic diseases with a common pathological origin. In rheumatoid arthritis, however, the cardiac lesions are likely to be less severe in character. Furthermore, the arthritic condition restricts the patient's activities; hence heart disease is tolerated relatively well.

A. Garland

210. **Cardiac Manifestations in Friedreich's Ataxia**

- G. W. MANNING. *American Heart Journal* [Amer. Heart J.] 39, 799-816, June, 1950. 7 figs., 10 refs.

Out of 6 cases of Friedreich's ataxia encountered by the author within a period of 2 years, 4 had an irregular tachycardia due to auricular or ventricular extrasystoles, and electrocardiographic changes resembling those caused by infarction. One patient died from heart failure, the heart showing post mortem only a diffuse fibrous, lymphocytic infiltration, with hypertrophy of the remaining muscle fibres.

D. Verel

211. **Employment of Supplementary Thoracic Leads in Diagnosis of Myocardial Infarction. (Do emprêgo de derivações torácicas suplementares para o diagnóstico do enfarte do miocárdio)**

- ADRIANO DE AZEVEDO PONDÉ and ALBERTO DE AZEVEDO PONDÉ. *Arquivos Brasileiros de Cardiologia* [Arch. brasil. Cardiol.] 3, 1-24, March, 1950. 24 figs., 41 refs.

Wilson (*Amer. Heart J.*, 1946, 32, 135) was the first to employ supplementary chest leads in electrocardiography; the electrodes are placed over the anterior and postero-lateral walls of the left hemithorax at a higher level than the conventional chest leads, and the tracings thus obtained are of value for the diagnosis of high myocardial infarcts, which may be antero-lateral, lateral, or postero-lateral.

The authors describe 5 cases of myocardial infarction in which the tracing from the conventional leads eventually returned almost to the normal configuration, so that it was difficult to be sure whether there had been an infarction or not. It was found that employment of supplementary leads made the diagnosis of infarction obvious. Several electrocardiograms are reproduced to illustrate the various points brought out. If changes suggestive of infarction are present in VL leads, then the authors believe that supplementary leads should be taken. In one case of high antero-lateral infarction a marked Q wave was found when the electrode was



placed over the second intercostal space on a level with V5 and V6. In 3 of the cases the infarct was of the high antero-septal variety, with the possibility of incomplete right bundle-branch block in one of them. Similar cases have been published in which the QRS configuration has returned to normal in the conventional leads; it is suggested that leads taken from more extensive areas would have revealed some abnormality. The authors conclude that these high leads are of definite value in the diagnosis of coronary thrombosis occurring at the base of the left ventricle.

Paul B. Woolley

**212. A Survey of the Cases of Morbus Caeruleus seen at the Children's Hospital, Zürich; the Diagnostic Difficulties.** (Étude d'ensemble des cardiopathies congénitales cyanogènes observées à l'Hôpital des enfants de Zurich et de leurs difficultés de diagnostic)

E. ROSSI, M. GROB, and M. BETTEX. *Helvetica Paediatrica Acta* [*Helv. paediat. Acta*] 5, Suppl., 49-84, July, 1950. 28 figs., 10 refs.

In this survey 88 cases of congenital malformation of the heart are discussed; they were studied clinically and investigated with the help of modern methods. To overcome differential diagnostic difficulties the authors recommend the morphological and chemical examination of the blood, capillaroscopy and examination of the eye-grounds, electrocardiography and phonocardiography, radioscopy, radiography (including barium swallow), and angiocardiology, measurement of the intracardiac pressure, determination of the oxygen saturation, and measurement of circulation time by the injection of fluorescein. None of these investigations should be omitted, for diagnostic errors would lead to fatal consequences in cases of surgical intervention.

Franz Heimann

**213. Functional Phlebtonometry.** (О функциональной флеботонометрии)

V. A. VAL'DMAN. *Клиническая Медицина* [*Klin. Med.*, Mosk.] 28, No. 5, 25-31, May, 1950. 5 figs., 11 refs.

Tests of cardiac function based on measurement of the arterial pressure and pulse alone do not give any indication of the state of the right ventricle. Right ventricular insufficiency is reflected in the venous pressure.

The author mentions methods of measuring this last, beginning with Tsypljaev's "bloodless" phlebtonometer (1903). This was inaccurate, and its use has been displaced by methods based on venipuncture. Moritz and Tabor employed a manometer filled with physiological saline, which flows into the vein until the pressures in vein and manometer are equal. (Originally 2% "chinosol" was used, but this was replaced by saline because of its toxicity.)

This method has largely been replaced in the Soviet Union by one in which blood is allowed to flow into the manometer, which is filled with water or, for prolonged observations (five or more minutes), with a 4% solution of sodium citrate. No extraneous fluid enters the circulation by this method, and the author states that it is safe and accurate and gives consistent readings. He claims that it does not record wide fluctuations in

pressure; as does the method of Moritz and Tabor; these fluctuations he regards as due to changes of tone in the vein caused by the injection of extraneous fluid.

He gives examples of its use, and records made with a photographic recording apparatus are reproduced showing the sensitivity and stability of the instrument. One such example is from a case of acute glomerular nephritis, in which the venous pressure at rest was observed to fall in the course of convalescence from 190 to 55 mm. of water; the effect of effort (Valsalva's method) was shown by a rise to 270 mm. at the beginning of the series of observations, but only by a rise from 55 to 130 mm. at the end, thus proving that circulatory function had improved. He also reproduces tracings demonstrating the fall in venous pressure after injection of 1 in 1,000 solution of nitroglycerin, and the rise after the administration of 1 ml. of 1 in 1,000 adrenaline.

The article is followed by the report of a discussion on the relative merits of the two instruments.

L. Firman-Edwards

## HYPERTENSION

**214. Diagnosis of the Initial Stages of Hypertension.** (К вопросу о диагностике начальных стадий гипертонической болезни)

I. A. RYVKIN and I. B. GUREVICH. *Клиническая Медицина* [*Klin. Med.*, Mosk.] 28, No. 5, 34-40, May, 1950. 2 figs., 25 refs.

The authors investigated 448 persons (126 men and 322 women) suffering from neither cardiac nor renal disease and with arterial blood pressures consistently below 140/90 mm. Hg. All the subjects were under 40 years of age. They underwent radiological examination in various projections, including the standard antero-posterior and oblique positions, with the object of detecting ventricular enlargement. Criteria are given of enlargement of the left ventricle.

They emphasize especially the importance of a triangle bounded in front by the lower border of the left ventricle; below by the diaphragm, and behind by the shadow of the inferior vena cava, seen normally in the left anterior oblique position; this triangle gradually disappears as the left ventricle enlarges. They accept Frey's standard, according to which the transverse diameter of the left ventricle in this position should not exceed by more than 1 cm. one-quarter of the diameter of the thorax, measured from the right border to the left costo-vertebral articulation at the corresponding level.

They found that 134 of their subjects showed left ventricular enlargement by these standards—10% of those under 20, 25% of those between 21 and 30, and 39.2% of those between 31 and 40. Separating these as a group, they found that, in contrast to the remaining 314, this group had a higher average systolic, diastolic, and mean arterial blood pressure and an increased lability in the response of these pressures to varying conditions (rest, exertion, and excitement). Tachycardia, accentuation of the aortic second sound, vasomotor instability, and electrocardiographic abnormalities (inverted or diphasic T waves in lead III) were commoner.

They followed up 186 of the 448 subjects over a period of 4 to 8 years; 33 showed hypertensive changes at the end of this period and of these, 30 were members of the special group referred to above. They consider that the figure 140/90 mm. Hg as a normal maximum blood pressure is too high, since the highest systolic pressure observed in the group with enlargement of the left ventricle was 131.9 and the highest diastolic pressure 78 mm. They regard lability of arterial pressure as one of the earliest signs of hypertension.

L. Firman-Edwards

#### 215. Dietary Treatment of Hypertension

H. UCKO. *British Medical Journal* [Brit. med. J.] 2, 144-147, July 15, 1950. 35 refs.

The effects of Kempner's rice diet (consisting of rice, fruit, and sugar) or a diet of identical composition except that the rice was replaced by pearl barley, and of a low-sodium diet were observed by the author in 14 unselected cases of hypertension, in 3 men and 11 women whose ages ranged from 35 to 72 years, 6 of whom were put on the rice diet, 5 on the barley diet, and 4 on the low-sodium diet. A fall in blood pressure and loss of body weight occurred in all cases, the changes being slightly greater on the average in patients on the rice diet, though the small number of patients makes it impossible to draw any significant conclusion. Patients initially given the rice or barley diets maintained the reduction in blood pressure satisfactorily when changed on to the low-sodium diet.

It is suggested that the effect of Kempner's rice diet and the barley diet is mainly due to its low content of sodium, the withdrawal of which creates a metabolic situation, probably through hormonal influences, in which high blood pressure cannot be maintained. By a close study of sodium intake and excretion the author found that minimal blood-pressure levels were maintained only when the daily intake of sodium was less than 250 mg.

S. Karani

#### 216. Clinical Effect and Functional Changes in Surgical Treatment of Hypertension. (Клинический эффект и патофизиологические изменения при хирургическом лечении гипертонической болезни)

E. N. ARTEM'EV. *Клиническая Медицина* [Klin. Med., Mosk.] 28, No. 5, 41-47, May, 1950. 6 refs.

A series of 39 patients were operated upon for hypertension, the operation consisting of resection of the greater and lesser splanchnic nerves and of the semilunar ganglia; operation was unilateral in 24 cases, but bilateral nerve resection was carried out in 12 and bilateral ganglionectomy in 3 cases. The cases are classified in five groups: grade 1, transitory or vegetative hypertension; grade 2, persistent hypertension without clinical signs of, or with only early signs of, arteriosclerosis; grade 3, with clinical signs, but no loss of organic function; grade 4, with early functional disabilities; grade 5, with definite organic dysfunction.

Out of 12 patients in grade 5, 8 were dead within a year, and 1 more within 15 months of operation. Of the remaining 3, one has had a stroke and the others have

well-established heart failure. Relief of symptoms occurred in 7 cases, but only temporarily. Out of this series, the arterial pressure in all cases had returned in 3 months to the pre-operative level.

Of 14 patients in grade 4, 5 died in 9 months. Symptoms were more often relieved than in the preceding group, but returned in those who survived up to 2 years, by which time only one patient had an arterial pressure lower than the pre-operative level. Of 13 patients in grades 2 and 3, none died within 2 years, but in only one patient was the arterial pressure lower than before operation by that time. Subjective improvement was more prolonged than lowering of arterial tension.

Lowering of pressure in the central retinal artery was observed in only one of the grade-5 cases, in 3 out of 5 cases in grade 4, and in 4 cases in grades 2 and 3 [the total number examined is not given].

Venous pressure was measured in 10 cases by Val'dman's method. In 6 it was raised before operation; in all these cases it fell nearly to normal after operation. [Further records after 1 to 2 years are not given.] In no case with electrocardiographic abnormalities before operation did these disappear.

Of those 14 patients who died, 6 died of uraemia; in 4 of these the urine had a specific gravity under 1018. The author regards lowered renal function with lowered specific gravity of urine as a contraindication to operation, but renal dysfunction with a normal or raised specific gravity of urine need not preclude surgical treatment. He concludes that sympathectomy will relieve symptoms in many cases, enabling patients to resume work, but that in cases with already well-developed arterial changes, sclerotic processes continue after operation and the symptoms return. Operation is contraindicated in cases in grade 5, and is of doubtful value in cases in grade 4. Cholesterol content of blood is slightly lowered in grades 3 and 4, but is unaltered in grade 5. Calcium and potassium levels are unaltered. Age in itself is no contraindication. Good results were obtained in 2 patients over 60 years old.

L. Firman-Edwards

#### 217. Evaluation of Surgical Treatment of Hypertension. (К оценке хирургического метода лечения гипертонической болезни)

A. M. SHPILEVSKAJA. *Терапевтический Архив* [Terap. Arkh.] 22, No. 3, 26-35, May-June, 1950.

This is a report on a series of 38 cases of hypertension treated by sympathectomy, 32 by removal of the sympathetic ganglia from the eleventh thoracic to the second lumbar and 6 by splanchnotomy. Most (25) of the patients were between 35 and 50 years old, and most gave a history of symptoms lasting for from 1 to 5 years.

Of the 25 patients with malignant hypertension 3 died within 24 hours of operation, 12 died between 1 month and 2½ years after operation, and 10 improved and resumed work, although one of this last group died 2½ years later after an operation for gastric ulcer. Of the 13 patients with benign hypertension, 11 were able to resume work, but 1 died 1 month, and 1 died 3 months, after operation. The longest periods of improvement noted so far are in one patient with malignant and one

with benign hypertension, both of whom have been at work for 3 years since operation.

It was found that patients with malignant hypertension benefited only when signs of cardiac disorder had not yet appeared. In the pre-operative and post-operative care of the patients, it is most important that they should be disturbed only as much as is essential.

Jeffrey Boss

#### 218. Pulmonary Hypertension in Chronic Pulmonary Emphysema

C. W. BORDEN, R. H. WILSON, R. V. EBERT, and H. S. WELLS. *American Journal of Medicine* [Amer. J. Med.] 8, 701-709, June, 1950. 5 figs., 32 refs.

Direct measurement of the pulmonary arterial pressure was carried out by means of catheterization in 24 men with chronic pulmonary emphysema who were moderately or completely disabled by effort dyspnoea. The average age of the group was 55, the range being 33 to 70 years. Pressure was measured by means of a Hamilton manometer and optically recorded. The degree of emphysema was estimated by measuring the total lung volume, vital capacity, and functional residual air.

The mean pulmonary diastolic pressure was  $22 \pm 7$  mm. Hg, and the range 15 to 37 mm. This was distinctly higher than in a group of 12 control subjects, in which the values were 8.8 and 6 to 11 mm. Hg respectively. There was no demonstrable correlation between the degree of pulmonary hypertension and the severity of the emphysema, but the average pulmonary arterial pressure was higher in 8 patients who had shown signs of right heart failure than in the others. On the basis of a normal arterio-venous oxygen difference and a normal oxygen consumption the authors concluded that the cardiac output was not raised in these cases. Again, they were unable to find any correlation between the degree of oxygen unsaturation and the arterio-venous oxygen difference.

Paul Wood

#### 219. Studies on the Circulation of Blood in Man. VII. The Effect of a Single Intravenous Dose of Theophylline Diethanolamine on Cardiac Output, Pulmonary Blood Volume and Systemic and Pulmonary Blood Pressures in Hypertensive Cardiovascular Disease

L. WERKÖ and H. LAGERLÖF. *Scandinavian Journal of Clinical and Laboratory Investigation* [Scand. J. clin. Lab. Invest.] 2, 181-197, 1950. 5 figs., 19 refs.

The effect of theophylline diethanolamine was studied in 11 cases of hypertensive cardiovascular disease. Four patients had congestive heart failure; in the remaining 7 the condition was considered "compensated" although one patient had dyspnoea on exertion and some others had an enlarged heart. The drug, in a 0.4-g. dose, was given intravenously or into the pulmonary artery over a period of  $1\frac{1}{2}$  to 2 minutes.

The important findings were as follows. The cardiac output usually increased (markedly so in the patients with heart failure) and the increase lasted for about 25 minutes. This effect is thought to be due to direct action of the drug on the left ventricular myocardium. The cardio-

pulmonary blood volume on an average decreased a little in the hypertensive patients with "compensation", but increased in the others. There was a consistent decrease of blood pressures in the pulmonary artery and pulmonary capillaries lasting for more than 25 minutes. This finding partly explains the efficacy of theophylline in cardiac asthma. No similarly consistent change was noted in the systemic blood pressure. Right auricular pressure decreased in most cases, but in others it did not change.

A. I. Suchett-Kaye

#### 220. Cortisone in Hypertensive Vascular Disease

G. A. PERERA, T. C. FLEMING, K. L. PINES, and M. CRYMBLE. *Journal of Clinical Investigation* [J. clin. Invest.] 29, 739-744, June, 1950. 1 fig., 7 refs.

A patient with uncomplicated benign hypertension received 200 mg. of cortisone daily for 30 days. There was a slight fall in blood pressure after a week, which persisted for 2 weeks after cessation of treatment. During the period of administration there were negligible changes in fluid, electrolyte, or carbohydrate metabolism, but a markedly negative nitrogen balance. Delayed healing of a breast abscess was noted while cortisone was being given.

D. Verel

#### 221. Observations on the Management of Hypertension by the Kempner Rice Diet

C. R. WILLIAMSON. *New England Journal of Medicine* [New Engl. J. Med.] 243, 177-182, Aug. 3, 1950. 4 figs., 10 refs.

This article from the Cushing Veterans Administration Hospital, Framingham, Massachusetts, describes in detail some interesting observations on 67 patients receiving the Kempner rice diet for hypertension. Only those subjects were chosen in whom the diastolic pressure (taken as the point at which sounds disappear on reducing pressure in the sphygmomanometer cuff) was above 100 mm. Hg. in repeated determinations by 2 observers. After a preliminary period of observation of 3 weeks without diet, and despite the fact that they were not confined to bed, 37 of the 67 were eliminated from the study as their diastolic pressure had fallen below 100 mm. Hg. The diet contained 200 g. (dry weight) of rice, with fruit, sugar, and fruit juices in sufficient quantities to provide 2,500 Calories and 1,000 ml. of fluid. Iron and vitamin supplements were also given.

After 19 more patients had been eliminated either owing to complications such as heart failure or because they could not stick to the diet, the remaining 11 were observed over 6 or more weeks. In all of these cases there was loss of weight and symptomatic improvement, but in 7 of the 11 cases no fall in diastolic pressure was observed. In the 4 cases in which a fall in diastolic pressure did occur, the addition of salt-free protein to the diet produced no change in blood pressure. Capsules were given to these 4 patients which on some occasions contained lactose, on others salt. In 3 cases the addition of 8 to 10 g. of salt daily to the diet produced a rise in the diastolic pressure, in 2 a rise in the systolic pressure, and in one no change in either. Withdrawal of the salt caused a return to the previous low level. Case histories



are given. The author points out the importance of the psychological and malnutritional aspects of the diet in contributing to its success.

G. S. Crockett

**222. Studies on the Influence of the Low Sodium Cardiac Diet and the Kempner Regimen on Renal Hemodynamics and Electrolyte Excretion in Hypertensive Subjects**

R. E. WESTON, L. HELLMAN, D. J. W. ESCHER, I. S. EDELMAN, J. GROSSMAN, and L. LEITER. *Journal of Clinical Investigation* [J. clin. Invest.] **29**, 639-650, June, 1950. 3 figs., bibliography.

A series of 9 patients with uncomplicated hypertension were maintained successively for short periods on a normal hospital diet, a low-salt cardiac diet, and a Kempner rice diet, in random order, and the effect on renal plasma flow, glomerular filtration, renal arteriolar resistance, maximum tubular excretion of *p*-aminohippurate, filtration fraction, plasma volume, and the serum sodium and chloride concentrations observed. On the low-salt diet, only a decrease in glomerular filtration rate was found. On the rice diet (with mercurial diuretics in several cases) the glomerular filtration rate fell in all cases and there were smaller reductions in renal plasma flow and in the filtration fraction. In 2 cases a rapid infusion of salt-poor serum albumin restored the renal plasma flow, but did not affect the glomerular filtration rate. The possible significance of the findings is discussed, but no definite conclusion is reached.

D. Verel

**223. The Relations of Essential Hypertension and Renal Disease in Pregnancy.** (К вопросу о взаимосвязи гипертонической болезни и нефропатии беременных)

N. L. STOTSIK and T. O. ORLOVA. *Клиническая Медицина* [Klin. Med., Mosk.] **28**, No. 5, 47-52, May, 1950.

Out of 250 pregnant women with hypertension, 27 were suffering from essential hypertension, and of these in 8 cases the disease was complicated by "pregnancy kidney". In these cases prognosis was poor.

A series of 49 patients, suffering from kidney disease of pregnancy, but not from essential hypertension when first coming under observation, were followed up for periods varying from 3 to 11 years; 26 of them sooner or later developed essential hypertension. Two types of evolution were noted; in the first, the disease began immediately after pregnancy, in the second there was a distinct interval of time.

The authors emphasize that pregnancy in normal women does not cause any rise in arterial blood pressure; in those predisposed to essential hypertension, however, a rise takes place early in pregnancy. In both groups arterial blood pressure tends to fall at mid-term, but, whereas in normal women it remains at low levels until the end of pregnancy, in the hypertensive type there is a fresh rise to abnormal heights in the second half of pregnancy. Hypertension is due to the toxic effects of substances elaborated by the foetus or placenta, not to mechanical pressure on renal vessels or ureters, since intrauterine foetal death results in diminution of toxæmia and fall in arterial pressure even before the extrusion of

the foetus. Tareev claims that of 29 women in whom hypertension followed prolonged gestation 16 developed malignant hypertension. Attempts to prolong pregnancy in the hope of obtaining a viable infant are utterly unjustifiable.

L. Firman-Edwards

**224. The Influence of Section of Splanchnic Nerves and Removal of the 1st and 2nd Lumbar Sympathetic Ganglia on Renal Function in Hypertension.** (Влияние перерезки чревных нервов и удаления 1-2 поясничных симпатических члеников на функцию почек при гипертонической болезни)

I. A. ITSIKSON. *Терапевтический Архив* [Terap. Arkh.] **22**, No. 3, 35-38, May-June, 1950. 8 refs.

This paper is based on the findings in a series of 11 cases of hypertension treated by splanchnotomy and lumbar ganglionectomy. Observations on renal function were made one month or less after operation, except in one case in which they were made 7½ months later. The author's figures do not indicate any marked post-operative change in renal function; he claims that glomerular filtration is increased post-operatively.

Jeffrey Boss

**225. The Relation of Hypertension to the Renal Circulation**

J. TRUETA. *Glasgow Medical Journal* [Glasg. med. J.] **31**, 217-242, July, 1950. 16 figs., bibliography.

**BLOOD VESSELS**

**226. Coarctation of the Aorta in Early Infancy**

M. M. CALODNEY and M. J. CARSON. *Journal of Pediatrics* [J. Pediat.] **37**, 46-77, July, 1950. 4 figs., 46 refs.

This is a report on 22 infants (13 male and 9 female) with coarctation of the aorta, on 21 of whom necropsies were held. The coarctation was of the adult type in 2 cases, combined adult and infantile in 5, and of the infantile type in the remainder. Seventeen of the infants were normal at birth, 2 were persistently cyanosed, and 3 intermittently so; 17 developed signs or symptoms of cardio-respiratory distress within 14 days of birth, and 18 died during the first 2 months. The blood pressure was raised in the upper extremities (systolic pressure ranging from 100 to 190 mm. Hg and diastolic from 70 to 130 mm. Hg) in 14 of the 17 cases in which it was recorded. Blood pressure could not be recorded in the lower extremities in 14 of the 17 infants. Femoral pulsation was sought for in 20 cases; it was absent in 10 and palpable in 10 (in 9 of which there was a widely patent ductus arteriosus). An inconstant systolic murmur was heard over the praecordium in 15 cases. Cyanosis was ultimately present in 19 cases, the liver was enlarged in 20, oedema was present in 14, and cardiac enlargement was demonstrated in 21. In 19 cases death was due to congestive cardiac failure. Associated minor congenital cardiac abnormalities were present in 12 cases, and major anomalies in 5 of the 21 examined post mortem.

The authors diagnosed the condition during life in 14 cases, on the basis of hypertension in the upper extremities with absent urinary and neurological findings. They recommend that routine blood-pressure estimation and femoral-pulse palpation should be undertaken in all newborn infants. The value of digitalis in treatment is discussed and the importance of infections in causing the onset of cardiac failure is stressed. *Wilfrid Gaisford*

**227. The Clinical Picture of Isthmic Coarctation of the Aorta in the First Months of Life.** (Das klinische Bild der Isthmusstenose der Aorta in den ersten Lebensmonaten)

S. BUCHS. *Annales Paediatrici* [Ann. paediatr., Basel] 175, 102-120, July-Aug., 1950. 17 figs., 11 refs.

The recent success of surgical treatment of congenital coarctation of the aorta has altered the approach to, and outlook in, cases of this malformation. Previously, expectation of life did not exceed 35 years and approximately 40% of those affected died between the ages of 15 and 35 years. As surgical treatment is best attempted at early school age the timely diagnosis of the disease has become vital. Operation before that time may lead to post-operative stenosis, but on the other hand delay increases the risk of aneurysm. Descriptions of the malformation in the literature have largely been confined to cases in adults or in children from the eighth year of age upwards, and little has hitherto been known of the clinical picture in infancy, the classical features being mostly of a secondary or tertiary nature and requiring some years to develop. Rib erosion (Roesler's sign) is not seen before the fifth year, and hypertension and arteriosclerosis develop much later.

On the basis of observations made during the last 6 years on 6 babies with isthmic coarctation of the aorta, a description of the clinical picture of this condition in infancy is presented. Three of the cases were diagnosed only post mortem, the other 3 during life, the diagnosis in 2 of these being verified post mortem and in the third case, in which the patient is still alive, by angiocardiology. There was no history of virus disease of the mother during the early months of pregnancy, but 5 of the infants were born in the years 1944-5 after a prolonged shortage of fat supplies, felt especially in the lower income groups to which the patients belonged. Reference is made to the animal experiments of Wilson and Warkany (*Amer. J. Anat.*, 1949, 85, 113) in which anomalies of the aortic arch were found in 30% of the offspring of rats fed on a vitamin-A-free diet. The babies looked well after birth, but developed signs of left and right heart failure, dependent upon the degree of stenosis and the residual power of the heart muscle, between 4 days and 2½ months later. Anorexia, fatigue, cyanosis, dyspnoea, tachypnoea, tachycardia, enlargement of the liver, oedema, and hypostatic pneumonia were the most prominent symptoms and signs on admission. There was a latent period of at least one month before any murmur became audible, the latter apparently originating in the collateral circulation.

As these cases show, the radiological appearance of the heart—of little diagnostic value in the older child or the adult—shows graduated changes in infancy, allowing

definite conclusions to be drawn. In the stage of primary decompensation the picture is hardly specific, there being a diffuse enlargement of the heart with marked pulmonary stasis, but if the child survives, the picture becomes gradually more typical, showing concentric hypertrophy of the left fourth arch and slight dilatation of the left ventricle. The pulmonary knob disappears and the shadow of the great vessels is pushed to the right and becomes slightly prominent, producing a boot-shaped heart silhouette—a picture not seen in any other acyanotic type of malformation of the heart. This characteristic appearance was observed in 5 babies at the age of 1 to 2 months.

The blood pressure was normal initially in the upper limbs, but hypertension was already apparent at the age of 2 years. In none of the author's cases was the femoral pulse investigated before admission, but it had probably been absent since birth: routine examination of the peripheral arteries during the first months of life would facilitate an early diagnosis. It is noteworthy that visible evidence of collateral circulation developed in one of the patients at the age of 2½ years, the earliest yet recorded. The electrocardiogram showed regression of the physiological right-sided preponderance within the first 3 months, but there was a delay in the development of left-sided preponderance, probably owing to the temporary stasis in the pulmonary circulation leading to hypertrophy of the right ventricle. Changes in the optic fundi were found to depend upon the degree and duration of the hypertension and were of considerable significance in prognosis.

The clinical picture as presented here is found in the more severe cases only, and milder cases with few symptoms may remain undiagnosed at this stage. The combination of coarctation with other multiple minor malformations of the heart which was found in these cases is taken as further proof of the intrauterine pathogenesis of the condition. *M. Dynski-Klein*

**228. Thromboangiitis Obliterans in Women. Possible Relation to Rheumatic Disease**

E. A. EDWARDS. *New England Journal of Medicine* [New Engl. J. Med.] 243, 290-294, Aug. 24, 1950. 13 refs.

Thromboangiitis obliterans in the female is recorded in the literature in only 35 cases. The author gives details of a further 6 cases, all in young women who smoked 15 to 20 cigarettes daily. Active rheumatoid arthritis was present in 2 of the cases, rheumatic fever with carditis in another, erythema nodosum and iritis in the fourth, erythema nodosum alone in the fifth, and iritis alone in the sixth. Two other cases are mentioned, in both of which disease of major peripheral vessels was present. The first is that of a woman who had rheumatoid arthritis and rheumatic fever, and the second that of a man who had rheumatic carditis. A suggestion is made that Buerger's disease may yet come to be included in the comprehensive group of diffuse collagen diseases, which at present includes acute disseminated lupus erythematosus, dermatomyositis, scleroderma, polyarteritis nodosa, rheumatic fever, and rheumatoid arthritis.

*Geoffrey McComas*

## Disorders of the Blood

229. **Essential Lymphocytophthisis. A New Clinical Entity in Infancy.** (Essentielle Lymphocytophtise. Ein neues Krankheitsbild aus der Säuglingspathologie) E. GLANZMANN and P. RINIKER. *Annales Paediatrici* [Ann. paediatr., Basel] 175, 1-32, July-Aug., 1950. 9 figs., 13 refs.

A "lymphatic reaction", characterized by an absolute and relative lymphocytosis in the peripheral blood, accompanies several diseases—for example, pertussis, infective mononucleosis, and mumps. In prognostically unfavourable cases the blood picture may suddenly revert to a lymphopenia, or there may occur a more gradual decline in the number of lymphocytes in the peripheral blood—described as "lymphocytophthisis"—in conditions in which pathological changes occur in lymphoid tissue, as in progressive tuberculosis of the lymph nodes and spleen, or in Hodgkin's disease, myelogenous leukaemia, and carcinomatosis of the lymph nodes. Toxic damage by excessive exposure to x rays or radium may lead to the same reaction, and anaphylactoid agranulocytosis is often combined with a leucopenia. Total alymphocytosis has been described by Fisher-Wasels (1929) in an adult patient who developed signs of pancreatic deficiency and stenosis of the small intestine in the course of a chronic dyspepsia; selective damage to the lymphocyte-producing tissue was postulated as the cause of the condition.

The authors report 2 cases of "essential" lymphocytophthisis in infancy. The most prominent feature of the disease was a severe thrush infection affecting the whole length of the digestive and respiratory tract, with several septic manifestations on the skin. The total leucocyte count was normal or only moderately diminished, but the proportion of lymphocytes varied from 9% to 11% in one case, and declined progressively from 15% to 2.5% in the other. Before death the monocyte count increased in one case, and in both there was a marked increase in the proportion of immature granulocytes, with the appearance of toxic granulations. The spleen and lymph nodes were not enlarged. The babies died at the age of 5 and 7½ months respectively, in a state of severe marasmus with bronchopneumonia.

The post-mortem findings were identical in the 2 cases, there being a generalized atrophy of lymphoid tissue in the intestinal tract, lymph nodes, and spleen. The lymphopoietic parenchyma was replaced by a hypertrophic reticular stroma, and the marginal and central sinuses were enlarged and filled with blood containing only a few leucocytes. There was a widespread oidiomycosis of the respiratory and intestinal tract, with multiple ulcerations and necrosis. The bone marrow was aplastic, only the megakaryocytes remaining normal. It is suggested that there existed primarily a constitutional weakness of the lymphoid tissue, reducing resistance to infection. The severe thrush infection may have caused

further depression of lymphopoiesis, resulting in lymphopenia or alymphocytosis, and leading finally to panmyelophthisis.

M. Dynski-Klein

230. **Fulminating Purpura with Factor-V Deficiency. Cure by Exchange Transfusion** (Purpura fulminans mit Faktor-V-Mangel und Heilung durch Blutaustauschtransfusion)

C. GASSER and G. DE MURALT. *Helvetica Paediatrica Acta* [Helv. paediat. Acta] 5, 364-391, July, 1950. 8 figs., 28 refs.

The authors describe 2 severe cases of purpura fulminans following scarlet fever in a 7-year-old girl and a 6-year-old boy. The clinical picture, the pathogenesis, and the treatment of purpura fulminans are discussed and the following points are emphasized:

In these 2 cases a severe disturbance of coagulation existed which was due to an acute insufficiency of Owren's factor V, which was combined in one case with an excess of antithrombin of the heparin-antithrombin type. The great increase in plasma cells of the reticulum and in eosinophils in bone marrow, as well as the increase in  $\gamma$  globulins in the blood electrophoresis—findings which, too, were made for the first time—point to an increased production of antibodies and to an allergic diathesis. The second patient could be saved when moribund by a complete blood-exchange transfusion, while repeated smaller transfusions in the first case were unsuccessful. The exchange transfusion alone assures complete removal of abnormal products and a sufficient supply of those products which were absent in the blood. Exchange transfusion appears to be the method of choice for the treatment of purpura fulminans.—[From the authors' summary.]

231. **Congenital Thrombocytopenic Purpura. Purpura Hemorrhagica in Pregnancy and in the Newborn**

R. D. EPSTEIN, E. L. LOZNER, T. S. COBBEY, and C. S. DAVIDSON. *American Journal of Medicine* [Amer. J. Med.] 9, 44-56, July, 1950. 4 figs., bibliography.

The authors review 39 cases from the literature of pregnancy complicated by thrombocytopenic purpura and describe 5 cases in patients of their own, one of whom had 3 pregnancies while under observation. Six of the 7 infants had thrombocytopenia at birth, 4 had petechiae, and 4 gastro-intestinal bleeding. All recovered; a normal platelet count was attained in 4 cases in from 2 to 4 months. In the total of 46 pregnancies the maternal mortality was 8.7% and the infantile mortality 26.1%. One-half of the children had congenital thrombocytopenic purpura, but within a few months all had normal platelet counts. No aetiological factor was unmasked, but the authors suggest that a substance which depresses platelet formation in the infant traverses the placenta from the maternal blood. The presence of



this substance is independent of the spleen, for splenectomy does not prevent the appearance of thrombocytopenia in the infant.

Henry Cohen

**232. Monocytic Leukaemia.** (La leucemia monocítica)

C. JIMÉNEZ DÍAZ, A. MORALES PLEGUEZUELO, and G. PANIAGUA RODRÍGUEZ. *Revista Clínica Española* [Rev. clin. esp.] **38**, 89-112, July 31, 1950. 42 figs., 42 refs.

The authors, who work in Madrid, give detailed accounts [with many good photomicrographs and coloured plates] of the findings in blood and marrow and at necropsy in 5 cases of monocytic leukaemia, together with the blood pictures in 2 further cases, one of which was probably of the type described by Naegeli. They discuss at length the aetiology, clinical characteristics, and pathology of monocytic leukaemia, dividing it into acute and subacute types and differentiating it completely from the reticulosis. The haematology of these seven cases is analysed and from the analysis a multiple origin of the monocyte is inferred, either from a non-differentiated mesenchymal cell or from a haemocytoblast.

René Méndez

**233. Studies on the Histamine Content of Blood, with Special Reference to Leukemia, Leukemoid Reactions and Leukocytoses**

W. N. VALENTINE, M. L. PEARCE, and J. S. LAWRENCE. *Blood* [Blood] **5**, 623-647, July, 1950. 5 figs., bibliography.

**234. Clinical and Pathological Features of Follicular Lymphoblastoma (Brill-Symmers Disease).** (Zur Klinik und Pathologie des follikulären Lymphoblastoms (Brill-Symmers))

G. A. MARTINI and H. WENDEROTH. *Zeitschrift für Klinische Medizin* [Z. klin. Med.] **147**, 235-260, 1950. 11 figs., bibliography.

This is a survey (with 188 references) of the present state of the follicular lymphoblastoma problem, together with a report on 5 cases personally observed by the authors. The follicular lymphoblastoma is the one lymph-node tumour which shows differentiation of follicles, and its demarcation from the reticuloses is difficult only when this specific feature is not clearly shown, or, on the other hand, when a reticulosis has not yet progressed to a marked loss of differentiation. The authors take the view that follicular lymphoblastoma is a possible intermediary stage between reticuloses and the different lymphosarcomas, Hodgkin's disease, and lymphatic leukaemia.

The course of the disease is chronic, and about one-half of all patients survive the first 5 years. The eventual prognosis is universally bad, although good results in prolonging life may be obtained by deep x-ray therapy; high dosages are required (3,000 to 5,000 r rather than 400 to 1,000). Development of malignancy is not always detected on biopsy, because the histological picture in different lymph nodes is not necessarily uniform, some having the appearance of a malignant tumour while others still show the typical picture of follicular lymphoblastoma. Clinically, an increase in

the erythrocyte sedimentation rate is an early sign of malignant change, even before emaciation and debility have set in, and possibly a rise in the basal metabolic rate may also indicate activity of a malignant type in the growth.

The main histological difficulty arises in the differential diagnosis from non-specific hyperplasia. Follicular lymphoblastoma is characterized by an increase in the number and size of follicles and their equal distribution over the centre and periphery of the lymph nodes. The follicles themselves are less uniformly round than normal, and have a dense surrounding wall of reticulin fibres in the periphery, with little reticulum in the centre; there is diffuse interfollicular lymphocyte infiltration and consequent disappearance of lymph sinuses. Lymphoblasts, rather than reticulum cells, are seen in the areas of active growth, and there is also infiltration of the capsules by small round cells. The increase in lymphoblasts rather than reticulum cells can be shown in direct smears from an affected lymph node, and giant cells can also be demonstrated very well by this technique. The authors do not consider that the so-called "mirror-image cells", which contain two nuclei, are specific, having also seen them, for example, in Hodgkin's disease and lymphosarcoma.

H. Lehmann

**235. Bi-monthly Periodic Fever with Lesions of a Diffuse Reticulosis.** (Fièvre périodique bi-mensuelle avec lésions diffuses de réticulose)

P. MOLLARET, I. BERTRAND, and H. MOLLARET. *Presse Médicale* [Pr. méd.] **38**, 669-671, June 14, 1950. 7 figs.

This is the case report of a patient with a periodic fever of the Pel-Ebstein type who ultimately developed cerebral signs. At necropsy diffuse reticulosis was diagnosed histologically.

John F. Loutit

## ANAEMIA

**236. Transplants of Bone Marrow in Clinical Practice.**

(К вопросу о пересадке костного мозга в клиннике) I. J. PINSKI and V. A. STEDADU. *Терапевтический Архив* [Terap. Arkh.] **22**, No. 3, 63-65, May-June, 1950. 4 refs.

Three patients suffering from chronic hypoplastic anaemia were each treated by 4 to 6 replacements of 2 to 3 ml. of sternal marrow by marrow from the sternum of a donor of suitable blood group. Such treatment, together with transfusions of blood and packed cells, led to a reticulocytosis in 2 cases, a rise in the erythrocyte count and haemoglobin concentration in 3 cases, increase in platelet count and reduction in bleeding time in 3 cases, and an increase in erythrocyte precursors in the sternal marrow in 1 case. The remissions in the disease have lasted for 19 and 2 months respectively in 2 cases, and the third patient had a remission for 1½ to 2 months after each treatment. These results are better than those due to transfusion alone. The authors attribute the effect of the marrow transplants to stimulation of haematopoiesis by breakdown products of the foreign cells.

Jeffrey Boss

237. **Macrocytic Hyperchromic Anaemia in Infants.** (L'anemia perniciosiforme del lattante)  
M. GERBASI. *Helvetica Paediatrica Acta* [Helv. paediat. Acta] 5, 299-312, July, 1950. 6 figs., 24 refs.

A series of 24 cases of macrocytic hyperchromic anaemia in infants attending paediatric clinics at Messina and Palermo is reported. The disease was of rapid onset in the first 14 months of life, with pallor, anorexia, stomatitis, a red tongue with loss of papillae, and occasionally oedema. The liver and spleen were usually enlarged and there was hypochlorhydria. There was invariably evidence of malnutrition. The erythrocyte count was between 1,500,000 and 2,500,000 and the haemoglobin level about 25%. The colour index was greater than 1.0, the mean corpuscular volume was increased, and the Price-Jones curve was flattened and showed a tendency towards macrocytosis. Megaloblasts were not seen in the peripheral blood, but bone-marrow biopsy showed megaloblastic hyperplasia. The indirect Van den Bergh reaction was positive. In 5 cases there was associated involvement of the pyramidal tracts, and in 2 further patients there were rigidity and tremor of an extrapyramidal type.

Neurological signs responded to treatment with liver injections, but not to administration of folic acid. The anaemia was successfully treated with a course of liver injections, there being no relapses. Undue prolongation of breast-feeding, iron deficiency, but principally a temporary lack of haematopoietic principle as a result of nutritional deficiency or infection are suggested as the aetiological factors.

[Neurological features excepted, these cases correspond closely to those described by Zuelzer and Ogden (*Amer. J. Dis. Child.*, 1946, 71, 211) and Hutchison and MacArthur (*Lancet*, 1949, 1, 916). The author's use of the term "perniciosiforme" is rather misleading in that, unlike the case of Peterson and Dunn (*Amer. J. Dis. Child.*, 1946, 71, 252), there were no relapses after treatment had ceased.]

Donough O'Brien

238. **Mortality from the Risk of Gastric Carcinoma among Patients with Pernicious Anaemia**  
J. MOSBECH and A. VIDEBAEK. *British Medical Journal* [Brit. med. J.] 2, 390-394, Aug. 12, 1950. 3 figs., 13 refs.

A follow-up study of 301 patients treated for pernicious anaemia at the Bispebjerg Hospital, Copenhagen, from 1928 to 1949, showed that the mortality rate was in close accord with that of the general population of Copenhagen of the same sex and age groups. Of these cases 222 were followed up for 10 years or more; the female patients were found to have the same chance of survival as normal females, whereas the males had a slightly, but not significantly, higher mortality. The causes of death in the whole group are tabulated. Deaths from carcinoma totalled 21, a figure which corresponds to the expected number of cancer deaths, but in a surprisingly high proportion of this group, namely, in 8 females and 6 males, the carcinoma was gastric in origin. The expected number of cases of gastric carcinoma in a similar sample of the general population is stated to be 5.2.

From a study of their own cases and the literature the authors conclude that, when gastric carcinoma develops in patients with pernicious anaemia, it does not usually occur in the fundus and upper part of the body of the stomach where the pathological changes of pernicious anaemia are localized. It is suggested that pernicious anaemia and gastric carcinoma may both result from achlorhydria.

L. J. Davis

239. **Diphyllobothrium Infestation and Anaemia in Great Britain**

J. C. HARLAND, J. G. HUMBLE, and P. G. MANN. *British Medical Journal* [Brit. med. J.] 2, 188-192, July 22, 1950. 6 figs., 19 refs.

The case here presented is stated to be the first to be recorded in Great Britain of a patient developing megaloblastic anaemia as a result of infestation with the fish tapeworm, *Diphyllobothrium latum*. The patient was a Finnish domestic servant, aged 22, who had lived in England for 2 years. She developed a macrocytic anaemia associated with megaloblastic erythropoiesis, as revealed by sternal puncture. A histamine-fast achlorhydria was also present. Microscopical examination of the stools revealed diphyllobothrium ova. Treatment with extract of male fern resulted in the expulsion of 2 tapeworms which were identified as *D. latum*. Disinfestation was followed by a reticulocytosis and a rise in haemoglobin level in the blood, and subsequent treatment with liver extract resulted in the restoration of a normal blood picture. The histamine-fast achlorhydria persisted, however.

The recent literature on tapeworm anaemia is briefly reviewed.

L. J. Davis

## HAEMOLYTIC ANAEMIA

240. **The Presence of Cold Haemolysins in Sera Containing Cold Haemagglutinins**

J. V. DACIE. *Journal of Pathology and Bacteriology* [J. Path. Bact.] 62, 241-257, April, 1950. 25 refs.

The author describes in detail experimental observations on the characteristics of cold haemolysins which were associated with high-titre cold haemagglutinins in 7 patients, 4 of whom had virus pneumonia (with an associated acute haemolytic anaemia in one case), one Raynaud's disease (with one episode of haemoglobinuria), one chronic ischaemic heart disease, and one bronchiolitis. The activity of the haemolysins is affected by changes in pH, and the antibody is readily adsorbed in acidified sera, but not in non-acidified sera. It is suggested that this is due to the fact that agglutination, which interferes with the adsorption of the haemolysin, takes place more readily in alkaline sera. The haemolysins are cold antibodies and, although they do not unite with erythrocytes at 37° C., they may readily cause haemolysis at room temperature. They are thermostable, but a labile component of fresh serum has to be present during both the cold and warm phases of the reaction. Maximum haemolysis is produced by chilling at 2° to 5° C., followed by warming to 30° C. Except for the effect of pH these haemolysins behave like those of the Donath-Landsteiner type. The erythrocytes of patients with nocturnal

haemoglobinuria are much more sensitive than those of normal persons to these haemolysins. By the use of such erythrocytes, the author found it possible to demonstrate the presence of cold haemolysins, and of cold agglutinins at low titre, in the sera of some normal people. He also found some evidence that an "incomplete" form of antibody may be found alongside the cold haemagglutinins.

[This is an important paper which should be read by all those interested in the haemolytic anaemias.]

Janet Vaughan

**241. Erythrophagocytosis in Hemolytic Disease of the Newborn. A Report of Twenty-five Cases**

M. B. COOPER. *Blood [Blood]* 5, 678-683, July, 1950. 2 figs., 9 refs.

Erythrophagocytosis has been reported before in the blood of infants with erythroblastosis. Thorough searching of blood smears showed that there was phagocytosis of erythrocytes by polymorphonuclear leucocytes in 25 out of 27 affected infants studied; the phenomenon was seen on the first day of life in 15 cases; in 8 it was seen only after blood transfusion. No erythrophagocytosis was found in the blood of 30 normal newborn infants. Evidently erythrophagocytosis is a mechanism for getting rid of injured cells in the blood-stream, but the sparseness of leucocytes showing phagocytosis suggests that the reticulo-endothelial organs do most of the work.

M. C. G. Israëls

**242. Acute Haemolytic Disease of the Newborn—Erythroblastosis Foetalis**

S. HEYMANN. *South African Medical Journal [S. Afr. med. J.]* 24, 576-582, July 15, 1950. 12 refs.

This article deals principally with the clinical aspects of erythroblastosis foetalis and is based on personal experience of 52 cases in the past few years. For convenience, three clinical types—hydrops foetalis, icterus gravis neonatorum, and haemolytic anaemia of the newborn—are distinguished, although it is pointed out that the underlying pathological process is the same in all and that intermediate types may occur. In hydrops foetalis, there is oedema and anaemia, but rarely jaundice, and the foetus almost invariably dies before, or within a few hours of, birth; treatment is of no avail. In icterus gravis there may be oedema and small ecchymotic haemorrhages, and the placenta, amniotic fluid, and vernix may be stained yellow. The liver and spleen may be enlarged. The icterus is not always present at birth, but develops almost immediately, the skin being a deep saffron colour within a few hours. Some of these infants may recover completely if treatment is started promptly, but unfortunately many sustain cerebral damage. The blood shows anaemia and erythroblastosis, an increase in leucocyte count, and often a reduction in platelet count. The serum bilirubin level may be markedly raised, the coagulation time increased, and bleeding time prolonged. The prothrombin content of the blood may be lowered considerably, so that haemorrhages complicate the picture. The cerebrospinal fluid is generally bile-stained and the urine contains bilirubin, while bilirubin

excretion is increased markedly in the stools. After 7 or 14 days the stool may become acholic owing to biliary obstruction due to fibrosis, atrophy, or atresia of the ducts or to the swelling of damaged hepatic cells. This is of a serious prognostic significance. In the author's series there were 3 such cases out of 52. Haemolytic anaemia of the newborn is probably frequently overlooked, since many mild cases occur. Immature erythrocytes are not a feature of the blood picture, and the spleen and liver are usually not enlarged. There is usually a mild jaundice.

The author recommends the routine determination of Rh status and antibody estimations in all young women during pregnancy, but pleads for tact in broaching the subject with the patient. With regard to obstetric management, each case should be considered on its merits and an effort made to prevent undue prematurity. Rh-negative women who show no evidence of sensitization should be allowed to go to full term. Mildly sensitized women should be delivered at full term and the infant treated expectantly. In more severely sensitized women it would possibly be justifiable to anticipate full term by 2 or 3 weeks. The method of delivery must be judged individually in all cases. Haemoglobin estimation should be carried out on the cord blood. The clinical assessment of the condition of the child at birth and the therapeutic measures available are discussed; in addition to simple and exchange transfusion, other measures must be taken to correct anaemia and also to counteract any hepatic disturbance and to guard against intercurrent infection, to which these infants are unduly susceptible.

Lilian Raftery

**243. Erythroblastosis Foetalis in a Set of Identical Twins. Comparison of Results with Replacement Transfusion and with Conservative Therapy**

H. A. AGERTY, R. S. WICKSMAN, and L. KACHER. *American Journal of Diseases of Children [Amer. J. Dis. Child.]* 80, 63-68, July, 1950. 2 figs., 5 refs.

The occurrence of erythroblastosis foetalis in identical twins offered a unique opportunity to compare the value of exchange transfusion with more conservative treatment. The mother, aged 25, had had one previous pregnancy which terminated in a live birth, and on that occasion, as on this during pregnancy, she was reported to be Rh-positive. Twin "A" weighed 6 lb. 9 oz. (3.0 kg.) and twin "B" 7 lb. (3.18 kg.), at birth, and both developed jaundice 12 hours after delivery. Twin A was the more icteric and had a palpable liver and spleen. As the blood findings supported the diagnosis of erythroblastosis foetalis, and both infants were found to be Rh-positive, the mother's blood was re-examined and found to be Rh-negative. Twin A was given a replacement transfusion through the great saphenous vein, withstood the procedure well, and his condition improved. Further small transfusions were required on the 6th and 9th days. Twin B, although originally less ill, progressed more slowly, and a sudden fall in the erythrocyte count on the 5th day necessitated an immediate transfusion of 75 ml. of blood. Twin A lost his jaundice and regained his birth weight more quickly than twin B, but on the other hand twin A had



a convulsion and twittings 12 hours after the exchange transfusion. Nine months later both infants were developing normally and twin B was, if anything, more advanced in motor function.

Further investigation showed that the twins' blood was of group A, Rh, Rh<sub>1</sub> (CDe, cDE), and the mother's of group A, Rh<sup>o</sup> (cdE), with anti-Rh<sub>c</sub> (anti-D) agglutinins. Technically, both infants and mother were Rh-positive, but the infants had three antigens, whereas the mother had only Rh<sup>o</sup>. This stimulated production by the mother of anti-Rh<sub>c</sub> agglutinins and consequently her blood behaved as though Rh-negative.

No final conclusion could be drawn, but the general impression was that whereas the child given the exchange transfusion had the poorer prognosis before treatment, it improved faster in the first month than the child treated conservatively.

Ronald S. McNeill

## HAEMATOPOIETIC SYSTEM

### 244. Myeloid Metaplasia

M. BLOCK and L. O. JACOBSON. *Journal of the American Medical Association [J. Amer. med. Ass.]* **143**, 1390-1396, Aug. 19, 1950. Bibliography.

Twelve cases of myeloid hyperplasia seen within a period of 18 months are described. In 2 cases the condition occurred as the terminal stage of polycythaemia and in 3 cases as a result of carcinoma with skeletal metastases; 2 cases were associated with tuberculosis, one case was due to sclerosis of the bone marrow, and 4 appeared to be "primary". The clinical and haematological features correspond well with those already described in the literature. The bone-marrow findings were variable; only in one case was myelosclerosis generalized, but in 6 of them one sternal puncture failed to produce enough cells to make adequate smears. In the hyperplastic marrow the erythroblast was the dominant cell, in marked contrast to the findings in leukaemia. The importance of hepatic and splenic biopsy examination in diagnosis is stressed. Extramedullary haematopoiesis was demonstrated by these methods in every case in which they were carried out. The differential diagnosis from leukaemia is discussed in detail. [This is a lucid review of a subject which often causes difficulty.]

P. C. Reynell

### 245. Multiple Myeloma: a Study of 24 Patients Treated with Radioactive Isotopes (P<sup>32</sup> and Sr<sup>89</sup>)

J. H. LAWRENCE and L. R. WASSERMAN. *Annals of Internal Medicine [Ann. intern. Med.]* **33**, 41-55, July, 1950. 16 refs.

This is a summary of the results obtained in the treatment of 24 cases of multiple myeloma seen in 10 years. Hitherto the treatment has been by administration of urethane or stilbamidine or by irradiation, but everyone is agreed about the uncertainty of the action of these agents. On the whole, solitary myeloma is less lethal than multiple myeloma, which seems to be fatal, whatever treatment is given, within about 2 years. Radioactive phosphorus and radioactive strontium in the

form of isotopes may well prove to be valuable additions to treatment. Radioactive isotopes are more easily given than is radiotherapy, and do not cause so much constitutional disturbance. The relief of pain and general symptomatic improvement seem more evident with isotopes than with radiotherapy. Some combination of isotope therapy with stilbamidine administration may improve the outlook in certain cases.

G. F. Walker

### 246. Plasma and Red Cell Iron Turnover in Normal Subjects and in Patients having Various Hematopoietic Disorders

R. L. HUFF, T. G. HENNESSY, R. E. AUSTIN, J. F. GARCIA, B. M. ROBERTS, and J. H. LAWRENCE. *Journal of Clinical Investigation [J. clin. Invest.]* **29**, 1041-1052, Aug., 1950. 3 figs., 30 refs.

Iron turnover in plasma and erythrocytes was studied in 5 normal subjects and 69 patients by intravenous injection of radioactive iron (<sup>59</sup>Fe). The amounts given did not significantly alter the concentration of iron in the steady-state systems involved.

In normal subjects the turnover rates agreed with figures of the normal erythrocyte life obtained by other methods. The average iron turnover rates were: for plasma, 0.35 mg. per kg. body weight per day; for erythrocytes, 0.26 mg. per kg. body weight per day.

Out of 19 cases of polycythaemia vera, untreated or in relapse, 17 showed plasma and erythrocyte iron turnover rates up to ten times the normal. The high rate of turnover of iron in erythrocytes cannot be explained merely by the increase in erythrocyte mass. Some additional factor must be involved, possibly a decrease in cell lifetime or a peculiar cellular iron-exchange. (London *et al.*, *J. biol. Chem.*, 1949, **179**, 463, studied one case of polycythaemia vera in which the erythrocytes contained labelled glycine, and found the cell life-span normal.) In one severe case of polycythaemia with a grossly enlarged spleen it was shown that radio-iron was not taken up in that organ. In the same case, as the tracer element disappeared from the plasma it was shown to appear *pari passu* in the bone marrow. In 6 cases of polycythaemia vera during successful treatment with radio-isotopes turnover rates were below normal. In three doubtful cases the diagnosis of polycythaemia vera was excluded because turnover rates were found to be normal.

In 6 cases of secondary polycythaemia, turnover rates were high but not nearly so high as those in polycythaemia vera; in contrast to the latter, the values corresponded to an almost normal turnover rate for the increased cell mass.

In 7 patients with chronic myelogenous leukaemia, 19 with chronic lymphatic leukaemia, and 2 with untreated pernicious anaemia, the plasma iron turnover rates were abnormally high; the high erythrocyte iron turnover rates found in most of these cases again indicate the possibility of rapid cell destruction. When one of the cases of pernicious anaemia improved on treatment, the turnover rate decreased towards normal. Six cases of refractory anaemia gave widely varying results whose significance is not certain.

P. Mestitz

## Respiratory Disorders

### 247. The Pathogenesis of Chronic Substantial (Hypertrophic) Emphysema

F. G. FLEISCHNER. *American Review of Tuberculosis* [Amer. Rev. Tuberc.] 62, 45-57, July, 1950. 2 figs., 23 refs.

The various theories put forward in the past to explain the occurrence of hypertrophic emphysema are critically examined, and the author concludes that Laënnec's original view that the cause is expiratory obstruction due to mucosal swelling and excess of mucus in the bronchi (the result of chronic bronchitis) is correct. Some bronchographic evidence is presented in support of this contention.

John R. Forbes

### 248. Terramycin in the Treatment of Pneumococcal and Primary Atypical Pneumonia

G. W. MELCHER, C. D. GIBSON, H. M. ROSE, and Y. KNEELAND. *Journal of the American Medical Association* [J. Amer. med. Ass.] 143, 1303-1308, Aug. 12, 1950. 9 figs., 5 refs.

A series of 18 patients with pneumococcal pneumonia and 7 with presumed virus pneumonia were treated with terramycin. The antibiotic was given orally in the form of the hydrochloride. The initial dose was 2 g. and this was followed by 1 g. 6-hourly for from 4 to 8 days. Some evidence of gastro-intestinal irritation appeared in 9 of the 25 cases. In none was the nausea, vomiting, or diarrhoea sufficiently severe to require stoppage of treatment. No serious toxic effects were noted. All the patients with pneumococcal pneumonia showed the characteristic features of lobar pneumonia, and a typed pneumococcus was isolated from the sputum. In none were pneumococci found in the blood. In 11 of the 18, terramycin administration was begun during the first 2 days of illness. With one exception there was a dramatic fall of temperature within 24 to 36 hours of the first dose. There were no relapses, and complete radiographic clearing occurred in all cases. The response in the 7 cases of primary atypical (virus) pneumonia was also satisfactory, the temperature falling rapidly and demonstrable clinical improvement being usually evident within a few hours of the first dose.

J. R. Bignall

### 249. The Treatment of Pneumococcal Pneumonia with Large Doses of Repository Penicillin Compared with Lower Doses of Penicillin: a Study of 686 Patients

H. F. DOWLING, M. H. LEPPER, and H. L. HIRSH. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 220, 17-22, July, 1950. 14 refs.

In the treatment of pneumonia due to pneumococcal infection a dose of 600,000 units of penicillin in oil and beeswax was administered twice daily to 238 patients. A similar dose of procaine penicillin in oil was administered to 45 patients. With this treatment the fatality rate was 5%. The results were compared with those obtained from the use of other forms of penicillin every

3 hours either intramuscularly or by mouth. In most instances 15,000 units were injected by the intramuscular route. The dose by mouth varied from 80,000 to 100,000 units. This series of cases consisted of 403 patients; it included a sub-group of 68 patients, most of whom received a single intramuscular injection of 300,000 units of procaine penicillin in oil with aluminium monostearate. The fatality rate in the second series was 5.4%.

When the statistics concerning both groups of cases were analysed, it was established that there was no substantial disparity either in the age distribution of the patients or in the incidence of bacteraemia and complicating diseases. Thus in the first group of cases 47% of the patients were more than 40 years of age and the fatality rate for these patients was 8%. In the second group the corresponding figures were 43% and 10%.

The curative effect exerted by procaine penicillin in oil and by penicillin in oil and beeswax is discussed; the authors conclude that similar results can be obtained by the administration of preparations which produce lower concentrations of the antibiotic in the blood. Perhaps better results could be achieved with large doses of an aqueous preparation of penicillin given at infrequent intervals, but it is difficult to assess the value of any form of penicillin when pneumonia is complicated by conditions such as hemiplegia, heart disease, and uraemia.

A. Garland

### 250. Dosage of Aureomycin in Primary Atypical Pneumonia

W. A. BLODGETT, J. H. KEATING, and G. J. COFFIN. *Journal of the American Medical Association* [J. Amer. med. Ass.] 143, 878-879, July 8, 1950. 5 figs.

From St. Luke's Hospital, New York, the authors report a trial in which 14 patients with acute primary atypical pneumonia were treated with aureomycin in daily doses of 1 to 1.5 g. for periods varying from 3½ to 10 days. The patients were acutely, but not critically, ill, and radiography showed evidence of pulmonary infiltration in all cases. Cold-agglutinin titres were diagnostic in 7, and it is reported that treatment with aureomycin tends to diminish the expected rise in titre. The diagnosis was also supported by the absence of response to a preliminary course of penicillin in all but 2 cases. With aureomycin 10 of the patients became afebrile at the end of 48 hours, and another 3 after 72 hours' treatment. One had a low-grade fever for 4 days after an initial response. No relapses were observed. Drug toxicity was minimal and toxic symptoms occurred in only 3 cases.

The authors conclude that the administration of small doses of aureomycin is justified in all but critically ill patients suffering from primary atypical pneumonia, but note that experience during seasons yielding cases of greater severity may cause them to modify this conclusion.

R. N. Johnston

251. **Chronic Non-specific Pneumonia and Bronchogenic Carcinoma (Comparative Bronchographic and Histological Studies).** (Хроническая неспецифическая пневмония и бронхогенный рак)  
S. S. VAL'. *Клиническая Медицина (Klin. Med., Mosk.)* 28, No. 7, 42-49, 1950. 2 figs., 5 refs.

The author believes that pathological changes in the bronchi caused by chronic non-specific pneumonia are often the basis of bronchial carcinoma. The neoplastic degeneration is preceded by proliferation and metaplasia of the bronchial epithelium.

The study of lesions of the bronchial tree is facilitated by post-mortem bronchography carried out before the removal of the lungs from the thorax. As an opaque medium the author uses a 40% aqueous suspension of barium sulphate. This examination often results in the discovery of foci of chronic pneumonia and pneumosclerosis.

The chronic inflammatory lesions consist of endobronchitis, mesobronchitis, and panbronchitis, sometimes also bronchiectasis and mucous polypi, with metaplasia of the cylindrical epithelium into stratified or even keratinized epithelium. The bronchial lesions keep up a chronic inflammatory process in the parenchyma, resulting in pneumosclerosis.

In cases of pulmonary metastases of extrapulmonary tumours there are no such inflammatory changes in the parenchyma and bronchi.

A. Orley

## 252. Alveolar Cell Tumors of the Lung

C. A. GOOD, J. R. McDONALD, O. T. CLAGETT, and E. R. GRIFFITH. *American Journal of Roentgenology and Radium Therapy [Amer. J. Roentgenol.]* 64, 1-19, July, 1950. 13 figs., 13 refs.

Alveolar-cell tumour of the lung is a rare neoplasm, only 52 cases having previously been described under various designations such as "primary multiple carcinoma", "alveolar-cell carcinoma", "columnar-cell carcinoma", and "pulmonary adenomatosis". This multiplicity of names has arisen from doubt about the point of origin of the tumour, as it is still debatable whether the pulmonary alveoli are normally lined by epithelium. In this condition, however, the thin inter-alveolar septa are unquestionably lined by columnar cells which form papillary projections into the alveoli, and the use of the term "alveolar-cell tumour" is therefore justifiable. The authors here report 12 new cases, 8 of which were treated by some type of pulmonary resection, and four found by a search of the post-mortem files of the Mayo Clinic. The ages of the patients varied from 30 to 62 years.

There is no typical radiological picture. The earliest x-ray finding is a small, poorly-defined area of consolidation resembling a pneumonitis. As the disease progresses it may involve more and more tissue until the entire lobe is involved and other centres of involvement become apparent either in another lobe of the same lung, or in the opposite lung. These nodules may become confluent and give rise to the appearance of a single large mass or of extensive consolidation. As regards symptomatology, cough, which may be unproductive, is a con-

stant feature. However, sputum is often present, and in 32% of the cases reported it was copious and of a white, frothy character. This type of sputum, associated with a pulmonary shadow, is suggestive of the diagnosis. Haemoptysis and staining is common, and dyspnoea is marked where the lung involvement is extensive. Bronchoscopy usually shows nothing of significance, but examination of the sputum or of bronchoscopic washings may enable a diagnosis to be reached. Cells from an alveolar-cell tumour are larger than the cells normally present in sputum and are frequently more irregular; the nuclei are not prominent and the cytoplasm is pink-staining and is occasionally distributed in a crescent around the nucleus. In several cases this crescent-shaped appearance has been so marked that the tumour cells have had the appearance of the cells of the squamous type of carcinoma. It is possible to be even more certain of the diagnosis when clumps of columnar cells, which have a free border of cytoplasm and in which the nuclei are not particularly irregular, are present.

Surgical resection is the only effective method of treatment available at the present time. It is as yet too early to evaluate the results in the authors' 8 treated cases, but one patient was alive and well 2 years after resection, another 6 months after operation, and a third 3 months after operation. One patient died 2 years after operation from causes unrelated to her alveolar-cell tumour. In addition, it was noted at necropsy in 2 patients who died after operation that there was no evidence of residual disease in the remaining pulmonary tissue.

L. G. Blair

## 253. Metastatic Pulmonary Malignancy: a Study of Factors Involved in Exfoliation of Malignant Cells

F. H. ELLIS, L. B. WOOLNER, and H. W. SCHMIDT. *Journal of Thoracic Surgery [J. thorac. Surg.]* 20, 125-135, July, 1950. 6 figs., 26 refs.

The finding of malignant cells in the sputum of patients with metastatic pulmonary neoplasms is relatively rare. Of 400 cases in which sputum was found to contain malignant cells, 16 were cases of metastatic lung tumour. In a control series of 488 cases in which miscellaneous conditions were present and examination of sputum for malignant cells was negative, there were 30 cases of metastatic lung tumour. Of 100 patients whose sputum was reported as positive during the period in which the 488 cases in the control group were examined, only 4 were considered to have metastatic tumours of lung. The percentage accuracy of sputum diagnosis among the total of 34 with metastatic lung tumours was only 11.8%.

In order to explain this low figure, histological sections were made of secondary tumours of lung removed at operation or at necropsy. The authors found that the bronchial epithelium frequently maintained its integrity over the surface of the metastatic tumour, even when bronchial involvement was extensive. The epithelium was frequently flattened and in some areas had undergone squamous change; but, because its protective function was maintained, there was little opportunity for malignant cells to exfoliate and be removed with the sputum.

John Borrie



# Digestive Disorders

## STOMACH AND INTESTINES

### 254. Abrasive Balloon for Exfoliation of Gastric Cancer Cells

F. G. PANICO, G. N. PAPANICOLAOU, and W. A. COOPER. *Journal of the American Medical Association [J. Amer. med. Ass.]* 143, 1308-1311, Aug. 12, 1950. 4 figs., 8 refs.

For the work described, a standard 16 F. double-lumen tube is used. One lumen is connected with a syringe and is used for gastric wash-outs and aspirations. The other lumen is connected distally to an inflatable balloon. The balloon is made of a condom, open at both ends, which is fixed round the tube by silk ties about 8 cm. apart. "To the external surface are tied by single slipped bowknots approximately 250 pieces of untreated braided silk arranged in a regular pattern about 3 mm. apart and cut to leave ends about 2 mm. long." When the balloon is inflated with 175 ml. of air it measures about 10 cm. long by 5 cm. in diameter.

Cells for microscopy were obtained in 4 different ways from 17 patients with gastric carcinoma, 10 patients with simple ulcers, 2 patients with polyps, 3 patients with gastritis, and 1 patient with no gastric disease. The routine smears made from the resting juice were negative for malignant cells in 12 out of 17 cases of gastric carcinoma, whereas smears made from gastric aspirations after the balloon had been in place for 30 minutes gave 11 positive results out of 17. Smears made from mucus adherent to the bristles of the balloon after removal gave 9 positive results out of 17, and smears made after washing the balloon in Ringer solution and centrifuging the deposit gave 14 positive results out of 17. There were no false-positive results.

[There are two difficulties in the cytological diagnosis of gastric cancer. It is fairly easy to find cancer cells in the 80 to 90% of cases in which the diagnosis is obvious on other grounds and the probability of a surgical 5-year cure remote. It is difficult to find cancer cells in the less common types which are almost impossible to diagnose with certainty by radiology or gastroscopy, but in which the prognosis is relatively good. Routine gastric wash-out has long been known to be useless in diagnosis, owing to digestion of cells. The value of the balloon can thus be determined only by taking difficult cases and then comparing results with those obtained after continuous lavage with an alkaline fluid.]

Denys Jennings

### 255. Benign Disease of the Antral Portion of the Stomach

C. A. FLOOD. *Gastroenterology [Gastroenterology]* 15, 399-406, July, 1950. 2 figs., 15 refs.

The term "benign antral disease" is used for the familiar nondescript pre-pyloric deformity which is so difficult to distinguish radiologically from carcinoma.

In this paper 42 consecutive cases are described, but only in 15 out of 42 was the diagnosis verified histologically. In the other 27 the diagnosis was based on a clinical follow-up of 6 to 24 months. [A benign clinical course for 2 years does not exclude carcinoma. Submucosal infiltrations often cause mild symptoms for several years before becoming frankly malignant.]

Of the 42 patients, 41 were over the age of 35 and 29 were males. The length of history ranged from one month to 50 years. Remissions and exacerbations occurred as in cases of peptic ulcer. Only 3 out of 42 had histamine achlorhydria; the remainder had normal amounts of acid in the gastric juice. The antral deformity was seen to develop in serial radiographs as a sequel to ulceration in 7 patients. In only 2 patients was the deformity seen to disappear, but the follow-up period was short.

The radiologist diagnosed carcinoma definitely in 1 patient and tentatively in 6, and refused to exclude it in 23. In the remaining 12 cases a benign lesion was diagnosed without qualification. In 16 cases an ulcer was found by radiological examination, but in only 6 by gastroscopy. In 4 cases the gastroscopist diagnosed an antral spasm, and in about half the cases the gastroscopist found a normal mucosa. In 8 out of the 15 patients whose stomachs could be studied histologically a gastric ulcer was found. In 6 of these 8 the crater had been demonstrated by the radiologist, but in only 2 out of the 8 could it be seen by the gastroscopist. One non-existent ulcer was diagnosed by the radiologist. In 7 patients the only possible cause of the radiological deformity was gastritis and erosions. The author believes that this must cause smooth-muscle spasm.

Denys Jennings

### 256. Sugar Metabolism and its Regulation in Relation to Symptoms after Gastrectomy. (Ricambio e regolazione glucidica nella patologia del resecato gastrico)

L. DE FELICE. *Archivio Italiano delle Malattie dell'Apparato Digerente [Arch. ital. Mal. Appar. dig.]* 16, 190-220, 1950. 3 figs., 39 refs.

After partial gastrectomy for peptic ulcer 10 to 15% of patients develop morbid symptoms. These are divided into four groups by the author: (1) Distension, nausea, and borborygmi immediately after consumption of a small meal, and faintness, sweating, and diarrhoea later—the "dumping syndrome". There is usually some degree of anaemia, and radiological examination shows a rapidly emptying stomach. (2) Vague nausea and abdominal pains, borborygmi, and anorexia associated with a good nutritional state, no anaemia, and a properly functioning stoma—psychoneurotic symptoms. (3) Dyspepsia, marked loss of weight, and depression, with hypochromic anaemia, hepatomegaly, and accelerated emptying of the stomach. These patients are hypochondriacal in outlook with regard to eating, but recover confidence

after careful dieting, with extra vitamins. (4) Persistent epigastric pain radiating to the back, despite good gastric function and a satisfactory state of nutrition; this is due to cholecystitis.

The blood sugar level was determined in 20 patients with post-operative symptoms of the above types after giving: (a) a carbohydrate meal consisting of 50 g. each of starch, sugar, and glucose, (b) adrenaline, 1 mg. intramuscularly, and (c) insulin 12 units. In patients of group (1) there was an initial hyperglycaemia after the carbohydrate meal, due to abnormal rapidity of delivery of carbohydrate to the intestine and its subsequent absorption. The response to adrenaline was moderate, and that to insulin less than normal. It is suggested that in this group the initial symptoms after ingestion of food may be caused by the arrival of hypertonic solutions of chyme in the intestine due to rapid emptying of the stomach, while the later symptoms are due to hypoglycaemia resulting from release of insulin. Patients of group (2) were characterized by an excessive hyperglycaemic response to injected adrenaline, indicative of imbalance in the vegetative nervous system. Those of group (3) showed a reduced response to the carbohydrate meal and to adrenaline (with a prolongation of the subsequent hyperglycaemia) and an increased sensitivity to insulin. This is taken to indicate that the primary cause of the symptomatology in this type of case is a hepatic dysfunction. Patients with symptoms as in group (4) showed no abnormalities in carbohydrate metabolism, but had obvious signs and symptoms of biliary disease.

James D. P. Graham

#### 257. Patterns of Response of Gastric Mucoprotein and Acid to Insulin; Correlation with the Underlying Disease in the Non-operated Stomach of Man

G. B. J. GLASS and L. J. BOYD. *Gastroenterology* [Gastroenterology] 15, 438-452, July, 1950. 3 figs., 42 refs.

The authors describe a simplified volumetric procedure for the estimation of mucoprotein in gastric juice. Using this method, they studied the patterns of gastric secretory response to insulin-induced hypoglycaemia.

Subjects were divided into three groups: normal subjects, those with gastric and prepyloric ulcer, and those with duodenal ulcer. It was found that normal stomachs responded to an injection of 16 units of insulin first by a rise in mucoprotein secretion (40 minutes after injection), and then by a rise in hydrochloric-acid secretion (60 minutes after injection). In cases of duodenal ulcer the response was similar, but with higher secretory peaks. In those with antral lesions an interesting "dissociated pattern" of response occurred; the secretion of mucoprotein increased, but not that of acid. It is considered that this supports the theory that whereas the secretion of mucoprotein may be stimulated by the action of insulin on the vagal nerve endings, the stimulation of acid secretion requires the preliminary liberation of a substance from the intact antral mucosa.

The authors intend to publish further evidence, from their studies on mutilated stomachs, which is said to lend additional support to this theory.

John Naish

#### 258. The Continuous Twelve-hour Nocturnal Gastric Secretion in Normal Individuals and in Patients with Duodenal Ulcer after a 24-hour Fast

E. LEVIN, J. B. KIRSNER, and W. L. PALMER. *Gastroenterology* [Gastroenterology] 15, 454-457, July, 1950. 4 refs.

In order to answer criticism that the high nocturnal secretion of acid observed in sufferers from duodenal ulcer might be a late response to the test meal customarily given at 5.30 p.m. in such cases, the authors report further tests carried out after a 24-hour fasting period.

They studied gastric secretion in 16 normal subjects and 16 patients with duodenal ulcer; the results demonstrate that under the new test conditions the basal gastric secretion in the latter group was still significantly greater than in the former.

John Naish

#### 259. Effects of $\beta$ -Diethylaminoethyl Xanthene 9-Carboxylate Methobromide ("Banthine") on Human Gastrointestinal Function

R. L. WALTERS, J. A. MORGAN, and J. M. BEAL. *Proceedings of the Society for Experimental Biology and Medicine* [Proc. Soc. exp. Biol., N.Y.] 74, 526-529, July, 1950. 4 figs., 4 refs.

A study was made of the effect of  $\beta$ -diethylaminoethyl xanthene 9-carboxylate methobromide ("banthine") on gastric secretion in 2 normal subjects and 8 patients with duodenal ulcer. Gastric secretion was studied by means of continuous aspiration of gastric secretion in the fasting subject before and after the oral administration of 100 mg. of the drug, aspiration being interrupted for 30 minutes after giving the dose. The volume of secretion was diminished, but no significant change occurred in gastric acidity. No difference in response was observed between normal subjects and patients with ulcer. Gastric motility was recorded in 2 patients with duodenal ulcer by means of an intragastric balloon connected to a water manometer; a marked reduction in motility was observed for approximately 2 hours following the oral administration of 100 mg. of the drug. Small-intestine motility was similarly recorded in 2 patients with regional enteritis from a balloon in the upper jejunum. A depression of intestinal motility lasting up to 2 hours was observed after the oral administration of 100 mg. of the drug. No undesirable side-effects other than dryness of the mouth were observed.

R. A. Gregory

#### 260. Gastric and Duodenal Ulcer. Cases Treated at the Medical Out-patient Department 1937-39 and 1946-49. [In English]

A. SETÄLÄ and A. TELKKÄ. *Annales Medicinæ Internæ Fenniae* [Ann. Med. intern. fenn.] 39, 113-128, 1950. 1 fig., 35 refs.

Cases of peptic ulceration among patients attending the Medical Out-patient Department at Helsinki University during the periods 1937-9 and 1946-9, numbering 968 of which approximately 83% were in males, have been analysed. Patients with peptic ulcer constituted 1.6% of all those attending during the former period, and 3.7% during the latter, so that an increased incidence in the general population is assumed. Of the pre-war group

62% had gastric ulcers, and of the post-war group 40%, the proportion of women being 23.9 and 20.8% respectively. The proportion of women among patients with duodenal ulcer was 6.3% before, and 12.5% after, the war.

The length of history before diagnosis averaged 6 years, and the age at diagnosis in males was 39 for duodenal ulcer and 45 for gastric ulcer; the corresponding ages in women were 40 and 49 respectively.

Figures are given concerning the radiological site of the ulcer in the 743 post-war cases; 59.6% of the ulcers were in the duodenum, 13.7% in the pyloric region, 15.8% at the angulus, and 8.3% in the middle of the lesser curve, with 1.1% elsewhere in the stomach.

Ewald test-meals were carried out on 160 patients in 1937-9 and 643 in 1946-9 and revealed the presence of achlorhydria in 9% and 11% of cases respectively. It is concluded that a single estimation is of no diagnostic value, and a similar conclusion is reached concerning the occult blood test, since only in 11.1% of 550 cases, mostly without previous dieting, was Weber's test positive. In the absence of obvious bleeding, anaemia was uncommon, only 1.7% of 544 patients tested being significantly anaemic. The follow-up records are incomplete. It is concluded that the incidence of peptic ulceration, particularly in the duodenum, increased during the war, possibly because of feeding troubles, but that in 1949 there were signs of a tendency to return to the pre-war level.

K. Gurling

#### 261. Experimental Peptic Ulceration with a Neuro-vascular Basis

R. L. BISHTON. *British Journal of Experimental Pathology* [Brit. J. exp. Path.] 31, 316-320, June, 1950. 11 figs., 9 refs.

In the Department of Pathology, Bristol University, 54 guinea-pigs were injected twice daily with pilocarpine, over a period of 2 to 5 weeks.

Acute ulceration or haemorrhages of the mucosa of the stomach or duodenum were later found in 26 animals, and in a few cases perforation occurred. The lesions had a capricious "map-like" distribution, suggesting a vascular basis with infarction. In the second experiment adult guinea-pigs were given 10 to 20 mg. of pilocarpine hydrochloride intramuscularly. After they had been killed 20 minutes later by coal-gas, colloidal silver iodide containing a trace of brilliant green was run into the descending thoracic aorta under a pressure of 80 mm. Hg until a whitening of the surface of the stomach was seen. In 19 out of the 20 guinea-pigs examined some areas of mucosa remained dark, even though the overlying peritoneal surface was injected with silver iodide. The organs were then fixed in an 8% aqueous solution of formalin containing 4% sodium acetate. The silver iodide was converted into metallic silver by means of photographic developer, and the specimens were examined histologically.

In the normal areas a network of capillaries invested the gastric tubules, but was absent from the infarcted areas. No distinct submucous network was seen in any of the preparations, and the vessels in the muscular layer were of characteristic type. In the submucous and

muscular zones, occasional short vessels were seen connecting arterioles and venules. Similar microscopical findings occurred in localized areas of duodenum. In 6 control animals no filling defects of the mucosa were observed.

Peter Harvey

#### 262. Haematemesis and Melaena

C. D. NEEDHAM and J. A. MCCONACHIE. *British Medical Journal* [Brit. med. J.] 2, 133-138, July 15, 1950. 23 refs.

The authors have analysed the case notes of 476 patients admitted to the medical wards of the Aberdeen Royal Infirmary on account of haematemesis or melaena, or of both, during the years 1941-8. The series is presumed to include only patients bleeding from peptic ulcers or erosions, all cases in which another cause was found having been excluded. Of the 476 patients, 66 died—a mortality of 13.9%. In 16 cases the patient died of complications of various types, and in 5 cases the patient was enfeebled by pre-existing disease elsewhere when haemorrhage occurred. The authors found that neither the existence of a history suggestive of peptic ulcer of more than one year's duration (obtained in 379 cases) or of previous haemorrhage, nor the type of ulcer found subsequently, bore any significant relation to mortality, which was equal in the two sexes irrespective of age. Of the 66 deaths, 54 occurred in patients aged 50 years or more.

All the patients were under the care of the authors, who judged the severity of bleeding by reference to the hourly pulse chart and repeated estimations of blood pressure and haemoglobin level. Recurrent haemorrhage is regarded as the most reliable warning of the seriousness of the case, as an eroded artery at the base of an ulcer is the usual source of this type of bleeding. The mode of medical treatment employed by the authors is not specified, but the limitations of medical treatment in cases with recurrent bleeding are stressed and closer co-operation between physicians and surgeons in such cases is strongly urged.

S. Karani

#### 263. Haemorrhage from Peptic Ulcer. A Report on 170 Cases

A. G. OGILVIE and I. O. B. SPENCER. *British Medical Journal* [Brit. med. J.] 2, 138-141, July 15, 1950. 5 refs.

The authors have analysed the findings in 170 cases of gastro-duodenal haemorrhage encountered and treated by them during the years 1941-8 at the Royal Victoria Infirmary, Newcastle-upon Tyne. In most of the cases the diagnosis was of duodenal ulcer, and in 133 of them it was made on clinical grounds alone. Of the 170 patients, only 4 died—a mortality of 2.4%—and these cases are reported in full. In view of their low mortality figure the authors emphasize the advantages of admitting this type of case into a general medical ward rather than to a special gastro-enterological unit which, they suggest, should be regarded as a centre for research and the treatment of cases requiring special skill and facilities.

Surgical aid was invoked by the authors on two occasions only. The essential features of their routine medical treatment are: (1) morphine on admission; (2) replace-



ment of fluid loss, usually by mouth and only exceptionally by the intravenous route; (3) regular fluid or semi-solid feeds at frequent intervals; (4) prompt, adequate, and accurately-timed blood transfusion, the need for this being determined by the patient's general condition and hourly pulse chart; (5) administration of ascorbic acid, 100 to 500 mg. daily; and (6) magnesium trisilicate powder to relieve pain.

[The authors' low mortality rate is very impressive and reinforces their argument, with which many will agree, that cases of gastro-duodenal haemorrhage should be treated in a general medical ward and that the essentials for successful treatment are strict attention to detail and close and continuous observation rather than the possession of special skill and facilities.] S. Karani

See also Sections Hygiene and Public Health, Abstract 8; Pathology, Abstract 129.

**264. Thyroid Treatment in Coeliac Disease.** (Thyre-oideamedikation vid coeliaki)

O. ELGENMARK. *Nordisk Medicin* [Nord. Med.] **44**, 1343-1346, Aug. 25, 1950. 2 figs.

The author, attracted by a recent theory connecting the coeliac syndrome with deficient thyroid function, treated 5 patients suffering from coeliac disease with thyroid extract after vitamin therapy had produced no significant change. Treatment with thyroid resulted in rapid improvement, with speedy increase in weight. Iodine, which had not been excreted in the urine before, appeared after thyroid therapy began. The author intends to study iodine metabolism in coeliac disease by means of isotopes. W. G. Harding

**265. Ulcerative Colitis**

F. H. LAHEY. *Review of Gastroenterology* [Rev. Gastroent.] **17**, 723-736, Sept., 1950. 1 fig.

Although the majority of cases of ulcerative colitis may be treated medically, the author advocates early ileostomy and preferably colectomy in a certain number. The mortality of ileostomy has fallen from 22.3% to under 4% in his series, because the operation has been undertaken earlier than formerly.

Indications for ileostomy are given, which include massive haemorrhage, malignant degeneration, joint infection, and anal rigidity [complications not commonly regarded as indications in Britain]. When a Rutzen or Torbot type of bag is used by the patient, a normal life can be resumed with the medical and social problem of ileostomy management much reduced. Since the prospect of restoring the normal anatomy is slight and ileo-rectal anastomosis improbable, colectomy is also urged. This is best done as soon as the ileostomy is established, the colon being removed as far as the sigmoid; 3 months later the remainder is excised by abdomino-sacral operation.

Colectomy will deal also with the insidiously developing malignant change which in the author's view takes place in 5% of all cases. Malignant change is independent of polyp formation, which occurs in about 6% of the total. K. Gurling

**266. The Treatment of Chronic Ulcerative Colitis with Sodium Hexadecyl Sulfate**

J. F. PRUDDEN. *Gastroenterology* [Gastroenterology] **15**, 426-437, July, 1950. 15 refs.

The therapy of chronic ulcerative colitis described was based on three findings: (1) that lysozyme is greatly increased in the stools in ulcerative colitis; (2) that this enzyme promotes ulceration of intestinal mucosa; and (3) that lysozyme is inhibited by alkyl sulphates *in vitro*.

A dose of 600 mg. of purified and recrystallized sodium hexadecyl sulphate was given orally 4-hourly day and night, together with retention enemas of 100 ml. of an 0.86% suspension of the drug morning and evening. Side-effects included a burning sensation in the epigastrium and nausea. There was often an increase in the number of stools, but this passed off in a few days. Twenty patients received courses of treatment lasting between 2 and 10 weeks. There were 12 remissions, 6 cases of improvement, and 2 cases of failure. Case histories are given in detail.

The author concludes that the results found were encouraging, the drug promoting mucosal healing by inactivation of lysozyme. No effect was observed on the cramp-like pains or, of course, on the emotional disturbances usually present in this disease.

J. Basil Rennie

## LIVER

**267. A Case of Hepatic Refractory Rickets.** (Hepatische rhachitis—een vorm van refractaire rhachitis)

F. A. WILLEMUNS and I. O. MEULEMANS. *Maandschrift voor Kindergeneeskunde* [Maandschr. Kindergeneesk.] **18**, 17-28, 1950. 9 refs.

This is the case history of a girl, aged 2½ years, with symptoms of active rickets associated with marked hepatomegaly and splenomegaly. Liver function tests gave grossly abnormal results. Since the symptoms of rickets were not influenced by routine therapeutic measures, and since other causes were excluded, the disease was considered to be of hepatic origin.

A. Middelhoven (*Excerpta Medica*)

**268 (a). Studies on the Use of Aureomycin in Hepatic Disease. I. Aureomycin Therapy in Acute Viral Hepatitis**

J. M. SHAFFER, J. D. FARQUHAR, J. STOKES, and V. M. SBOROV. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] **220**, 1-5, July, 1950.

**268 (b). Studies on the Use of Aureomycin in Hepatic Disease. II. The Effect of Aureomycin on Experimental Dietary Hepatic Necrosis**

P. GYÖRGY, J. STOKES, W. H. SMITH, and H. GOLDBLATT. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] **220**, 6-11, July, 1950. 2 figs., 15 refs.

These two papers, part of a series not yet complete, deal with the effects of aureomycin treatment in hepatic disease. [A full assessment of the results must obviously await the publication of the whole series, for the experimental observations, based on an interesting hypothesis, are not yet ended.]

Aureomycin, in doses of 2 to 4 g. daily by mouth for 6 to 10 days, was administered to 37 patients suffering from acute infective hepatitis; 37 patients on the same general routine treatment, but without aureomycin, were used as controls. It was found that the drug exerted little if any effect on the length and severity of the acute phase of the disease, judged clinically and confirmed by a number of the regular tests of hepatic function. There was, however, a suggestion that some of the later effects of the disease might be influenced and controlled.

This led the authors, who are all working on behalf of the Commission on Liver Disease of the U.S. Armed Forces Epidemiological Board, Washington, D.C., to frame a hypothesis which seemed worthy of investigation. Could hepatic injury—either due to viral hepatitis or of nutritional origin—be accentuated by entry of micro-organisms or their metabolites from the intestine, and could aureomycin by its action on the intestinal flora prevent this?

Both papers deal with experimental dietary necrosis in rats and its delay or prevention when aureomycin was administered. The experimental results gave good support for the hypothesis, and further reports must be awaited with great interest. For instance, only 2 rats out of 20 in the control group survived and did not develop hepatic necrosis in 200 days, whereas 11 rats out of 22 given aureomycin survived for the same period. Further work is evidently planned on the effects of aureomycin in conditions of acute hepatic failure and coma, and in cases of chronic disease of the liver in which no clinical improvement has been achieved by ordinary treatment for several months. *J. W. McNee*

**269. On Certain Aspects of the Treatment of Liver Disease with Lipotropic Substances.** (Su di alcuni aspetti della terapia lipotropica delle epatopatie)

A. GAMBIGLIANI ZOCOLI and F. BUFFA. *Minerva Medica* [Minerva med., Torino] 41, 953-966, June 16, 1950. 26 figs., 39 refs.

Exact knowledge of pathology as a basis of treatment is nowhere more important than in liver disease, and especially in cirrhosis, with which this paper is chiefly concerned. The authors divide cirrhosis into two main types: (a) mesenchymal, characterized by hepatosplenomegaly without oedema or ascites, positive flocculation reactions, and hyperglobulinaemia, and histologically by interstitial fibrosis, and (b) parenchymal, in which there are retention of body fluids, a low plasma protein concentration, especially of albumin, and changes in blood cholesterol level and hippuric-acid synthesis, with degeneration of liver cells. The latter category is further subdivided into fatty and non-fatty types. The mesenchymal type is equivalent to the classical Laënnec's cirrhosis, may be the result of toxic or dietary factors, and is improved by the administration of lipotropic substances; the parenchymal type, in which there is a diffuse fibrosis cutting off small islands of degenerate cells, may be the chronic stage of a true viral hepatitis and does not respond to lipotropes. In some cases there may be conversion of a parenchymal into a mesenchymal

form of the disease, the course becoming consequently slower and more benign, although the fibrosis persists indefinitely.

A series of 22 patients with hepatic disease were given a standard diet and treated with a compound containing choline 2 g., methionine 2 g., and vitamin-B complex. Two cases of post-hepatic syndrome improved on this regime, but not appreciably more rapidly than a control case not treated with the compound; similar results were obtained in 2 cases of mesenchymal cirrhosis. In the fatty type of parenchymal cirrhosis less equivocal results were obtained, 5 out of 11 patients being free from signs or symptoms of disease nearly a year after treatment, but the non-fatty type (4 cases) did not respond. It is interesting to note that a patient with pernicious anaemia which did not respond to liver treatment was given lipotropic substances with dramatic response. From the biochemical view-point the appearance of a positive nitrogen balance, a rise in plasma albumin level, and an increase in sodium excretion are valuable indications of success in therapy. There is also some correlation between liver function and the total plasma protein content as expressed in grammes per sq. m. of body surface, which the authors state to be a more reliable indication than the commonly estimated percentage values. Those patients with an initially high total protein level generally do well, while in no case in which a favourable response was obtained in this series was the serum albumin level diminished by more than 17% of normal.

[The interest of this paper lies in the attempt to correlate symptomatic, biochemical, and histological patterns with therapy in liver disease.] *A. Paton*

**270. Portal Cirrhosis: an Analysis of 444 Cases with Notes on Modern Methods of Treatment**

B. E. DOUGLASS and A. M. SNELL. *Gastroenterology* [Gastroenterology] 15, 407-425, July, 1950. 1 fig., 31 refs.

An analysis is made of 444 cases of portal cirrhosis, the diagnosis being proved in 32.9% by operation, necropsy, biopsy examination, or peritoneoscopy. Males outnumbered females in the ratio of 3.5 to 1, and the highest incidence was in the 5th and 6th decades of life.

As aetiological factors, alcoholism was present in 64%, syphilis in 8.1%, and antecedent jaundice in only 3.6%. No causal factor could be found in 19.6%. The most frequent complaints were of abdominal distension, jaundice, bleeding from the alimentary tract, oedema, and abdominal pain, in that order. The commonest initial complaints were of abdominal enlargement, jaundice, abdominal pain, and haematemesis. On physical examination hepatomegaly was found in 70.9%, ascites in rather less than half the cases, and splenomegaly in 32.2%. As the majority of the patients died at home, it was possible to determine the cause of death in only 85. Of these, 50% died of massive haemorrhage from the alimentary tract and 30% in coma. Inter-current infection was very rare.

The patients were in the care of various clinicians, but invariably a highly nutritious diet with abstinence from

alcohol was recommended, together with intensive polyvitamin therapy, emphasis being laid on administration of the B complex. Less than one-third were treated in hospital, and the average duration of stay was only 3 weeks. The authors agree with the view that a diet rich in protein may safely contain at least enough fat to render it palatable. They found little evidence of vitamin deficiency in portal cirrhosis, and were not impressed by the results of giving liver extracts. Other therapeutic measures are discussed.

Fewer than half of the 84% of patients traced survived for more than 2 years; 11 survived for more than 7 years. Ascites, and to a lesser degree icterus, were unfavourable signs. A serum albumin level of less than 3.0 g. per 100 ml., marked retention of bromsulphalein, or a low level of cholesterol ester in serum were of grave significance.

Since there has been little increase in the time of survival from that found in two earlier surveys of portal cirrhosis at the Mayo Clinic, the authors conclude that prolonged stay in hospital under close supervision is probably an essential factor if the results of treatment are to be improved.

J. Basil Rennie

#### 271. The Relation of the Regenerated Liver Nodule to the Vascular Bed in Cirrhosis

R. H. KELTY, A. H. BAGGENSTOSS, and H. R. BUTT. *Gastroenterology* [Gastroenterology] 15, 285-295, June, 1950. 5 figs., 21 refs.

The effect of cirrhosis on the intralobular circulation of the liver is discussed.

There have always been doubts about this matter. The authors believed that growth of the regenerative nodules (nodular hyperplasia), and not pressure by contracting fibrous tissue, might be chiefly responsible for the vascular distortion. They thought that a three-dimensional study of a small mass of cirrhotic liver might give important information, and a three-dimensional model was made from a block of tissue obtained from a woman who died aged 24, and in whom the liver was small and cirrhotic.

[The details of the method are somewhat complicated and should be consulted in the original paper.] Briefly, sections 15  $\mu$  thick were cut and stained, and every tenth section was projected on to a sheet of paper at a standardized magnification of 15. The vessels and the regenerative nodules were outlined on the glass in different colours, and thereafter the glass plates were placed one on top of the other with a sealing medium between to exclude air. Finally the authors had two glass blocks, one made up of 20 sheets and the other of 18. From these glass blocks showing the outline of the vessels in colour, a wax model was carefully constructed. Examination of the wax model confirmed the belief that in cirrhosis the veins in the hepatic lobule are not compressed by fibrous tissue, but by the growing nodular hyperplasia. The larger vessels are not greatly distorted, but the smaller veins are compressed, narrowed, and twisted, and their direction within the lobule is changed.

J. W. McNee

See also Sections Pathology, Abstract 140; Medicine: General, Abstract 199.

## PANCREAS

#### 272. Dissociation of Secretion of Pancreatic Enzymes and Bicarbonate in Patients with Chronic Pancreatitis

M. H. F. FRIEDMAN and W. J. SNAPE. *Gastroenterology* [Gastroenterology] 15, 296-303, June, 1950. 16 refs.

A double secretin test, by the technique of Lagerlof (1942), was carried out on 8 patients in whom direct inspection at operation had revealed chronic pancreatitis. In 3 cases the second injection was of secretin combined with insulin. The results obtained were compared with those in 39 observations on 22 healthy persons as controls.

It was found that in the earlier stages of chronic pancreatitis the volume of pancreatic juice after secretin injection may be normal, but the concentration of enzymes is low. Later in the disease the actual volumes of enzymes and of bicarbonate are both diminished. A dissociation between the secretion of enzymes and of bicarbonate was noted, suggesting that the two substances are secreted either by different cells or that the disease acts selectively on the pancreatic tissues. The authors refer to previous work on this point by Grossman and Ivy, which suggested that the enzymes are secreted by the acinar cells and the bicarbonate and water by duct cells.

Insulin did not increase the output of enzymes in chronic pancreatitis as it does in normal individuals.

J. W. McNee

#### 273. Adenoma of the Islands of Langerhans. Its Differentiation from Functional Hypoglycaemia

H. A. PERKINS, J. F. DESFORGES, and C. G. GUTTAS. *New England Journal of Medicine* [New Engl. J. Med.] 243, 281-285 Aug. 24, 1950. Bibliography.

The case is described of a middle-aged Jewish woman who had typical attacks of spontaneous hypoglycaemia. An islet-cell tumour in the tail of the pancreas was removed, with complete relief of symptoms. The authors emphasize the difficulty in differential diagnosis between the islet-cell tumour and functional hypoglycaemia. The former gives rise to attacks of hypoglycaemia both in the fasting state and also 2 or 3 hours after a meal, whereas in functional hypoglycaemia the attacks do not occur in the fasting state. A low fasting blood sugar level of the order of 50 mg. per 100 ml. is the rule with islet-cell tumours, but a low value may also, though rarely, be found in functional hypoglycaemia. Glucose tolerance and insulin tolerance tests are of doubtful value in distinguishing between the two conditions, and the adrenaline tolerance test is also unhelpful. The most important distinguishing feature is the effect of fasting on the blood sugar level; the fast may have to be maintained for as long as 24 hours in order to induce an attack of hypoglycaemia.

The treatment of functional hypoglycaemia is with a high-protein, low-carbohydrate diet. Failure to respond to this regimen indicates that the patient probably has an islet-cell tumour and calls for exploration of the pancreas. If no tumour is found it is recommended that subtotal resection of the pancreas be undertaken. A mild permanent diabetes may result.

Geoffrey McComas



## Endocrine Disorders

274. **The Significance of the Adenohypophysis, Adrenal Cortex and Thyroid in Renal Function in Man.** [In English] R. LUFT and B. SJÖGREN. *Acta Endocrinologica (Copenhagen)* [Acta endocrinol., Kbh.] 4, 351-362, 1950. 25 refs.

Pituitary and thyroid insufficiency are associated with a decrease in glomerular filtration rate and renal blood flow. This also occurs in adrenal cortical insufficiency but the decrease in renal blood flow is relatively less. The authors investigated the effect of administering salt and deoxycortone (desoxycorticosterone) acetate and thyroid extract on renal function in a series of patients with pituitary insufficiency, Addison's disease, myxoedema, and acromegaly. Salt and deoxycortone caused a rise in glomerular filtration rate, but no corresponding increase in renal blood flow in patients with pituitary and adrenal cortical insufficiency. Thyroid extract caused an increase in renal blood flow and sometimes in glomerular filtration rate in pituitary insufficiency and myxoedema. In acromegaly the renal function was generally normal.

A. C. Crooke

275. **Influence of Cortisone and ACTH on the Mechanism of Infection.** [In English] J. ØRSKOV. *Acta Pathologica et Microbiologica Scandinavica* [Acta path. microbiol. scand.] 27, 770-772, 1950. 1 ref.

276. **Clinical Trials of ACTH. Preliminary Report** J. J. R. DUTHIE. *Edinburgh Medical Journal* [Edinb. med. J.] 57, 341-364, Aug., 1950. 30 figs., 5 refs.

277. **Treatment of Hyperthyroidism with 1-Methyl-2-mercaptoimidazole** W. S. REVENO and H. ROSENBAUM. *Journal of the American Medical Association* [J. Amer. med. Ass.] 143, 1407-1408, Aug. 19, 1950. 3 refs.

The drug 1-methyl-2-mercaptoimidazole ("tapazol") was administered over a period of 6 months to 18 hyperthyroid patients, 6 of whom had previously received no antithyroid treatment, 10 had been under control with propylthiouracil, and 2 were in relapse a year and a half after stopping thiouracil. With an initial dose of 2 to 5 mg. of tapazol every 8 to 12 hours there was a satisfactory response, and maintenance doses varied from 2 to 8 mg. daily. Tapazol resembled propylthiouracil in its action, but had a potency approximately 25 times greater. No toxic reactions were observed in this small series.

G. Ansell

278. **Observations on the Treatment of Thyrotoxicosis** I. MURRAY. *British Medical Journal* [Brit. med. J.] 2, 80-84, July 8, 1950. 2 figs., 19 refs.

Experience with methylthiouracil treatment is described in 142 cases of thyrotoxicosis observed for a minimum

period of 18 months. In 85 cases a satisfactory remission was obtained, and 76 of these patients remained well for a year or more after stopping treatment; in 7 a partial thyroidectomy was performed (in 6 cases at the patient's request, for cosmetic or other reasons, and in one case because methyl thiouracil repeatedly caused a severe leucopenia); 50 were still receiving the drug. The series included 21 cases in relapse after an earlier thiouracil-induced remission; 11 of these patients were again able to stop treatment, 8 for a year or more. Relapses after thyroidectomy were difficult to control and apt to recur; only 3 out of 14 such patients were able to stop treatment. Out of 15 patients with auricular fibrillation, in 8 rhythm reverted to normal with methylthiouracil alone, and in 3 with methylthiouracil and quinidine. There were 2 deaths, one almost certainly due to agranulocytosis, the other following a severe epistaxis; in the latter case treatment had been stopped because of leucopenia, which nevertheless persisted until death 12 months later.

The importance of emotional factors in determining the onset and response to treatment of thyrotoxicosis is emphasized. Continuing emotional disturbance was always found in cases difficult to control. Seven illustrative case histories are given. Observations were also made on a further 93 patients who had nervous symptoms and a goitre, but were not regarded as having thyrotoxicosis. A family history of thyrotoxicosis was obtained almost as commonly in these (11.8%) as in the frankly thyrotoxic group (15.3%), and it is suggested that in this type of patient psychiatric treatment might avert the later development of thyrotoxicosis.

[No indication is given of the dose of methylthiouracil or of the duration of treatment.] H. McC. Giles

279. **Treatment of Thyrotoxicosis with Radioactive Iodine**

E. S. GORDON and E. C. ALBRIGHT. *Journal of the American Medical Association* [J. Amer. med. Ass.] 143, 1129-1132, July 29, 1950. 3 figs., 14 refs.

The results in the first 120 cases of hyperthyroidism treated with radioactive iodine (<sup>131</sup>I) at the Wisconsin General Hospital and followed up for from 5 to 33 months are described. The ages of these patients ranged from 12 to 76 years. The only patients rejected for this treatment were those with very large goitres or pressure symptoms, and pregnant women. Dosage was based on gland size and toxicity. Treatment was planned to induce gradual remissions by the use of repeated small doses spaced at 3-monthly intervals, in order to avoid hypothyroidism. After a first dose averaging 3 millicuries 59 patients became euthyroid; 36 patients required 2 doses, 16 had 3 doses, and 9 patients required 4 or more treatments.

Results were satisfactory in practically all the cases, but 3 patients became hypothyroid, 3 had a subsequent

thyroidectomy for various reasons, and 2 were lost to follow-up.

The sensitivity of the thyroid to radiation varied in different patients, but there was no consistent difference in response between diffuse and nodular goitres. Shrinkage in size of both types of goitre often amounted to more than 50%. Four patients had normal pregnancies after or during treatment and the infants were normal.

G. Ansell

**280. Changing Pathogenesis of Addison's Disease, with Special Reference to Amyloidosis**

W. M. O'DONNELL. *Archives of Internal Medicine* [Arch. intern. Med.] 86, 266-279, Aug., 1950. 4 figs., 23 refs.

An analysis of 2,550 necropsies carried out at Ann Arbor from 1895 to 1928 revealed 7 cases of Addison's disease due to tuberculosis, one to cytotoxic necrosis, and one to amyloid disease. In 9,000 necropsies carried out between 1929 and 1949 there were 8 cases due to tuberculosis, 6 to cytotoxic necrosis, and 3 to amyloidosis. The article includes illustrations of amyloidosis and histoplasmosis of the adrenal gland. G. S. Crockett

**281. The Adrenal Cortex following ACTH: a Preliminary Report**

W. M. O'DONNELL and S. S. FAJANS. *University of Michigan Medical Bulletin* [Univ. Mich. med. Bull.] 16, 169-172, July, 1950. 1 fig., 8 refs.

An opportunity to study the adrenal cortex after ACTH (adrenocorticotrophin) administration arose when a woman with myeloid leukaemia and diabetes mellitus died 5 days after a 22-day course of 2,825 mg. ACTH. There were hypertrophy and hyperplasia of cortical cells with loss of lipids from the zona fasciculata, but an increase in lipids in the zona glomerulosa. These changes are ascribed to the ACTH treatment. S. S. B. Gilder

**282. Adrenal Insufficiency in Infancy. A Clinical Classification, Review, and a Report of a Case**

L. J. GEPPERT, W. A. SPENCER, and A. M. RICHMOND. *Journal of Pediatrics* [J. Pediat.] 37, 1-22, July, 1950. 5 figs., bibliography.

A case is reported of pure adrenal insufficiency in respect of the "S" factor (the steroids controlling sugar metabolism) in an infant observed from birth until its death at 20 months. The authors suggest that the cause of the deficiency was that translation from the foetal type of cortex to the normal adult type was incomplete, resulting in cortical hypoplasia, though it may have been the result of neonatal haemorrhage. The first symptom was vomiting, which began soon after birth. Pigmentation was noticed at 6 months and this increased steadily. After an acute illness at 8 months, which turned out to be roseola infantum, the child progressed well until 13 months, when he had an acute febrile attack, with vomiting and convulsions. He responded to treatment with glucose-saline intravenously and adrenal cortical extract intramuscularly. Thereafter he was given deoxycortone acetate, and extra salt in his diet. Attacks of diarrhoea, vomiting, and listlessness occurred at intervals and he finally died in coma at the age of 20

months. Necropsy showed that the adrenal glands were small (left 1 g. and right 1.5 g.); the medulla of each had developed normally, but with the neonatal involution of the foetal cortex the adult cortex had failed to develop and only a trace of the zona fasciculata (the site of origin of the "S" factor) was found. Liver and striated muscle showed complete absence of glycogen.

Examination of the blood during life revealed the low sodium and high potassium content characteristic of adrenal insufficiency. As regards carbohydrate metabolism, the oral glucose tolerance curve was flat. Random blood specimens showed low normal sugar levels, with immediate hypoglycaemia during periods of stress. During his terminal crisis 10% glucose given intravenously was insufficient to maintain a normal blood sugar level. The pigmentation observed resembled that of sun-tan and increased noticeably during periods of stress and dehydration. The authors believe this to be the first reported case of adrenal insufficiency unassociated with intersexuality. Wilfrid Gaisford

**283. Effect of Cortisone and Adrenocorticotropin Therapy on Serum Proteins in Disseminated Lupus Erythematosus**

M. REINER. *Proceedings of the Society for Experimental Biology and Medicine* [Proc. Soc. exp. Biol., N.Y.] 74, 529-531, July, 1950. 2 figs., 5 refs.

**284. The Effect of Combined Administration of Deoxycortone Acetate and Ascorbic Acid on Pathologically Disordered Muscle Function.** (Die kombinierte Desoxycorticosteronacetat-Ascorbinsäure-Anwendung in ihrer Wirkung auf die pathologisch gestörte Muskelfunktion) H. TEWES. *Ärztliche Wochenschrift* [Ärztl. Wschr.] 5, 595-597, Aug. 18, 1950. 9 refs.

**285. A Clinical and Biological Study of 29 Patients Treated with Adrenocorticotrophin.** (Étude clinique et biologique de 29 malades traités par la corticostimuline) F. COSTE, F. DELBARRE, G. BASSET, and F. LACRONIQUE. *Semaine des Hôpitaux de Paris* [Sem. Hôp. Paris] 26, 3047-3074, Aug. 30, 1950. 19 figs.

Adrenocorticotrophin (ACTH) was prepared from ox or sheep pituitary by extraction with acetone, bringing the pH to 11, and boiling [details of the method are given in a separate paper by Coste and Delbarre (*Sem. Hôp. Paris*, 1950, 26, 3033)]. From 10 to 80 mg. (average 40 mg.) was given daily in divided doses for periods of 1 to 3 weeks, after a control period of observation in hospital, to 29 patients with various diseases. Inert substances were substituted at intervals. Eight patients with rheumatoid arthritis were treated; in the 4 male patients the response was striking, although one was already in a state of advanced cachexia and amyloidosis and died in uraemia in spite of remarkable improvement in the joint condition. Of the 4 female patients, 2 responded well, though one relapsed while still under treatment; the other 2 responded only partially. One case of ankylosing spondylitis responded well, but relapsed on cessation of treatment, and one case of psoriasis arthropathica improved, with some regression of the skin lesions. In 6 cases of rheumatic fever there

was a striking response in the joint condition and a fall in temperature; pericarditis, which was present in 2 of these cases, was also improved, though it was doubtful whether there was any other effect on the carditis.

Marked improvement was obtained in acute attacks of gout in 3 cases. In one atypical case of chronic lymphatic leukaemia, which had entered into an acute phase, there was an improvement in the patient's general condition, and lymphoblasts disappeared from the peripheral blood and diminished in numbers in the marrow. A temporary response was obtained in a case of acute disseminated lupus erythematosus, with disappearance of the "butterfly" eruption and of the changes in the optic fundi, but the condition soon relapsed, the patient dying in uraemia. A slight degree of improvement was obtained in a case of dermatomyositis. In 4 cases of asthma the response was good, but in one of them a more severe attack followed the cessation of treatment. No response was obtained in one case of ulcerative colitis and one of pemphigus.

Side-effects from the administration of ACTH were not marked. The main effect was temporary water retention, sometimes associated with transient hypertension and tachycardia, but this subsided either spontaneously or after initiation of a salt-free diet and administration of salts such as ammonium chloride (to eliminate sodium), whether the ACTH was continued or not. Some increase in weight and rounding of the facial contour was noted in 2 patients, in one of whom, a man, there was increased facial hirsuties. Permanent hypertension was not induced in any case.

Robert de Mowbray

#### 286. The Effect of Adrenocorticotrophic Hormone in Panhypopituitarism

F. C. BARTTER, P. FOURMAN, F. ALBRIGHT, A. P. FORBES, W. M. JEFFERIES, G. GRISWOLD, E. DEMPSEY, D. BRYANT, and E. CARROLL. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 950-971, July, 1950. 12 figs., 28 refs.

Some effects are described of adrenocorticotrophin (ACTH) on 3 patients with panhypopituitarism. On a standard (analysed) diet the urinary excretion of nitrogen, phosphorus, calcium, potassium, chloride, sodium, and 17-ketosteroids and, in some cases, of other steroids was measured, together with the faecal output of nitrogen, phosphorus, calcium, and potassium. From these multiple balance data, and from changes in blood levels, it was possible not only to determine the net balance of the substances studied, but also to assess changes in their distribution within the body. The methods of calculation are described in this paper, or in earlier papers referred to in it.

The authors' main findings were as follows:

- (1) Nitrogen balance was negative, because the "sugar" hormone of the adrenal inhibited protein anabolism.
- (2) There was a loss of calcium, which might be due to osteoporosis comparable to that of Cushing's syndrome.
- (3) There was a loss of potassium and phosphorus. This may have represented a loss of intracellular fluid made available by the diminished formation of protoplasm, the effect being partly masked, so far as external balance of these ions is concerned, by retention of these

ions during glycogen deposition under the influence of the "sugar" hormone. (4) There was a transient loss of sodium and chloride, with subsequent retention; this may have been a pitressin effect. (5) There was a rise in corticoid excretion in the urine, and a less consistent rise in 17-ketosteroid excretion.

[For details, and for a just assessment of the evidence, the original paper should be consulted.]

D. A. K. Black

#### 287. Pituitary Basophile Hyperplasia and Crooke's Hyaline Changes in Man after ACTH Therapy

A. GOLDEN, P. K. BONDY, and W. H. SHELDON. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N. Y.*] **74**, 455-458, June, 1950. 1 ref.

The authors report the histological findings in the pituitary glands of 2 patients suffering from chronic glomerulonephritis who received adrenocorticotrophic hormone therapy (ACTH). The first patient was a 43-year-old man who received a total dose of 400 mg. He died 5 days after starting treatment. The adrenal glands weighed 18.5 g. together. The pituitary gland showed striking hyaline cytoplasmic changes, and a differential count demonstrated a significant increase in the relative number of basophil cells.

The second patient was a 19-year-old woman who received 490 mg. of ACTH in 8 days and died 7 days later. The adrenal glands also weighed 18.5 g. together. Hyaline cytoplasmic changes were present in only a few scattered basophil cells, but a differential count again demonstrated a significant increase in the relative number of basophil cells. The interpretation of the hyaline basophil change is discussed in the light of these findings.

A. C. Crooke

#### 288. Further Clinical and Experimental Studies on the Pathogenesis of Cushing's Syndrome

P. HEINBECKER and M. PFEIFFENBERGER. *American Journal of Medicine* [*Amer. J. Med.*] **9**, 3-23, July, 1950. 6 figs., 36 refs.

The authors accept only three primary causes for Cushing's syndrome—adrenal cortical tumour, a tumour of the ovary secreting progesterone, and atrophy of the paired paraventricular hypothalamic nuclei. In this paper they record 2 cases illustrating the first and the last. [They evidently regard the association which has been recorded of other tumours, such as thymic carcinoma, with Cushing's syndrome as coincidental.] From pathological and experimental evidence they suggest that atrophy of the paraventricular hypothalamic nuclei leads to overactivity of hypophyseal eosinophil mechanism and depression of the basophil secretion, thus running counter to what is the accepted teaching on pituitary basophilism.

[Their views are difficult to reconcile with the known effects of eosinophil excess—gigantism and acromegaly—and the occurrence of Cushing's syndrome in basophil adenocarcinoma of the pituitary. This paper does not lend itself to effective summary, but deserves to be studied despite its heterodox views.]

Henry Cohen



## Dermatology

289. **Vitamin E in Dermatology.** (La vitamin E, con speciale riferimento alla dermatologia)

G. STERZI. *Archivio Italiano di Dermatologia, Sifilografia e Venereologia* [Arch. ital. Derm.] 23, 257-285, 1950. Bibliography.

Daily doses of 50 to 250 mg. of  $\alpha$ -tocopherol (average 150 mg.) were given for 1 to 4 months to 25 patients with lupus erythematosus who had all been unsuccessfully treated by other means previously. "Clinical cure" was defined as an absence of recurrence within 6 months after finishing the course. Of the 25 patients, 13 were clinically cured; in 2 the condition improved slightly, in 4 it proved refractory to treatment, 4 patients became worse, and 2 suffered a recurrence during the observation period. In 9 out of the 12 cases unsuccessfully treated with  $\alpha$ -tocopherol, combined treatment with gold and histamine resulted in clinical cure. Excellent therapeutic results are also claimed with  $\alpha$ -tocopherol in varicose eczema, acrocyanosis, cutis marmorata, purpura, and alopecia areata, while moderate success is reported in rosacea, erythema induratum, lichen planus, malum perforans pedis, kraurosis vulvae, scleroderma, and certain occupational dermatoses.

[The first 20 pages of this paper deal with the general physiology of vitamin E and only 9 lines are allotted to the treatment of the 12 last-named dermatological conditions.]

Z. A. Leitner

290. **Protection of the Skin from Sunburn. Comparison of the Absorption Spectra of Screening Agents and their Efficacy in Eczema Solare**

B. RUSSELL and D. ANDERSON. *Lancet* [Lancet] 2, 247-250, Aug. 12, 1950. 4 figs., 13 refs.

In most skin diseases caused by the sun's rays, the wave-lengths concerned lie between approximately 2,900 and 3,300 Å. Urticaria solare, however, is usually due to rays of 3,900 to 5,200 Å. Because window-glass screens all rays of wave-lengths shorter than 3,130 Å it gives complete protection [sic] against most of these disorders but none against urticaria solare.

The authors performed several tests of screening agents, incorporated in different bases, on a male, aged 58, who suffered from eczema solare. They found that an area of skin could be completely protected against exposure to the rays emitted from a mercury-vapour lamp by a thin film of ointment containing "lanette wax SX" 6.25%, liquid paraffin 6.25%, and yellow soft paraffin 87.5%. The screening effect of this base they attribute to the high percentage of soft paraffin. Four different substances—tannic acid 5%, quinine hydrochloride 5%, sodium *p*-aminobenzoate 10%, and salol 10%—were incorporated in five different bases. It was found that aqueous solutions and suspensions of the screening substances were all ineffective; that ointment of wool alcohols is very effective when screening agents are added;

and that soft yellow paraffin is effective for the purpose but that its screening properties are lessened by the addition of tannic acid 5%, or quinine hydrochloride 5%.

The absorption spectra of various creams were determined with a Hilger quartz spectrograph, a high-voltage spark from metal electrodes being used as a source of light. These experiments indicated that in these creams the part played by the vehicle is as important as that of the screening agent. The most successful base used in conjunction with sodium *p*-aminobenzoate was pasta hamamelidis B.P.C., but this base may be "cracked" by other screening agents such as tannic acid. The authors therefore recommend the following as a non-greasy substitute with suitable cosmetic properties: stearin 25, triethanolamine 1, glycerin 10, oil of theobroma 1, cetyl alcohol 0.5, and distilled water 62.5, dispensed in an airtight container. The incorporation of tannic acid 5%, quinine hydrochloride 5%, "pyribenzamine" 5%, sodium *p*-aminobenzoate 10%, or salol 10% in this emulsion was found to be either "effective" or "relatively effective", the first three sun-screens on this list being the most satisfactory.

The authors discuss the dangers which may arise from contact eczema provoked by the use of sun-screens. They regard tannic acid as the most innocuous sun-screen, and recommend that sodium *p*-aminobenzoate should not be employed if the patient has previously been sensitized to sulphonamides or to benzocaine.

Solar urticaria cannot be prevented by the use of these "chemical parasols", because they give no protection against the group of rays concerned; for the prevention of this malady, physical screens such as calamine, titanium dioxide, or ichthammol must be used. The authors give two suitable formulae.

R. M. B. MacKenna

291. **Solar Dermatitis**

J. H. LAMB, B. SHELMIER, Z. COOPER, R. J. MORGAN, and C. KEATY. *Archives of Dermatology and Syphilology* [Arch. Derm. Syph., Chicago] 62, 1-27, July, 1950. 10 figs., bibliography.

The authors find solar dermatitis common among outdoor workers, and note that fluorescent lighting may provoke or aggravate the condition in indoor workers. These dermatoses cannot be classified according to the activating wave-length of the radiations or according to age at onset. Classification into three groups is suggested, the first consisting of polymorphic light-sensitive eruptions, the second of urticarial rashes, and the third of rare types, such as hydroa aestivale.

Periods of immunity may be observed in patients suffering from these dermatoses, and different regions of the body may not be equally sensitive. The type of reaction may change in the same patient. Patch tests to weeds did not suggest that they played an important part in light sensitization. Histological appearances are described at length.

Injection of gonadotrophic hormone from pregnant mares' serum gave promising results in male patients under 50 years of age.

John T. Ingram

**292. The Inhibitory Effect of Three Antihistaminic Compounds on the Growth of Fungi Pathogenic for Man**  
L. E. CARSON and C. C. CAMPBELL. *Science [Science]* **111**, 689-691, June 23, 1950. 1 fig., 4 refs.

Finding that several cases of tinea pedis responded dramatically to treatment with a cream containing 2% tripeleannamine hydrochloride ("pyribenzamine"), the authors examined 3 crystalline antihistaminic compounds to determine whether their effect was only against the allergic manifestations of the aetiological agent or whether they were also fungistatic or fungicidal. The compounds tested were tripeleannamine, antazoline ("antistin"), and "diphenylpyraline". They were examined at concentrations of 0.1 to 1.0 mg. per ml. against a range of organisms including 8 strains of *Trichophyton*, 7 of *Epidermophyton floccosum*, 4 of *Microsporium*, and single strains of *Candida albicans*, *Cryptococcus neoformans*, *Histoplasma capsulatum*, and *Blastomyces dermatitidis*.

Diphenylpyraline completely inhibited the growth of all strains at a concentration of 0.5 mg. per ml., and the effective concentration of antazoline varied from 0.5 to 1.0 mg. per ml. Tripeleannamine was the least effective; concentrations of 1.0 mg. per ml. failed to inhibit 13 of the 23 organisms. Higher pH values enhanced the activity of tripeleannamine, but at pH 5.0 all the compounds were inactive. Diphenylpyraline was the most effective in the presence of serum, but antazoline was inactive at both pH 5.0 and pH 7.0. The authors conclude that both diphenylpyraline and tripeleannamine are worth studying further to evaluate their activity against fungi *in vivo*.

Malcolm Woodbine

**293. Endemic of Infection with *Microsporium audouinii* in a Family of Eight Persons**

A. G. FRANKS, E. H. MANDEL, and A. S. STERNBERG. *Archives of Dermatology and Syphilology [Arch. Derm. Syph., Chicago]* **62**, 54-57, July, 1950. 1 ref.

In one family two adult members had lesions due to *Microsporium audouinii* infection on smooth skin and one child had an infection of the eyelashes. In two children the scalp was involved.

John T. Ingram

**294. Lichenoid Tuberculid. A Clinical and Histopathologic Study**

O. E. OCKULY and H. MONTGOMERY. *Journal of Investigative Dermatology [J. invest. Derm.]* **14**, 415-426, June, 1950. 6 figs., 10 refs.

Detailed individual reports on 13 cases of lichenoid tuberculid are given. The authors believe that what they call lichenoid tuberculid is a subgroup of haematogenous forms of cutaneous tuberculosis. Lesions may occur anywhere on the skin, but are commonest on the limbs and usually symmetrically distributed. No lesions of mucous membranes have so far been seen. The predominant lesion is a non-pruritic, flat-topped, or slightly umbilicated papule, the size of a split pea, violaceous to brown, with overlying and peripheral telangiectasia, and

capped as a rule by a fine adherent scale. Macular lesions may be seen. Papules are discrete and grouped, occasionally coalescing. Annular configuration is often noted. On involution brownish macules remain, but no scars.

The histological changes are those of a haematogenous tuberculosis with typical tubercle formation and varying degrees of caseation necrosis. In 3 cases there was no caseation and the picture resembled that of sarcoidosis.

The condition may be confused with lichen planus, lichen nitidus, or even purpura. It is frequently associated with tuberculosis of lymph nodes or systemic tuberculosis, but the skin lesions are essentially benign and apparently respond to treatment with gold sodium thiosulphate.

James Marshall

**295. The Relationship of Host and Virus in Molluscum Contagiosum**

G. RAKE and H. BLANK. *Journal of Investigative Dermatology [J. invest. Derm.]* **15**, 81-93, Aug., 1950. 9 figs., 14 refs.

The changes occurring in infections of human epithelial cells with the virus of molluscum contagiosum were studied histochemically and with the electron microscope. The first changes were an increase in ribose nucleic acid synthesis and enlargement of the nucleolus. Islets of desoxyribose nucleic acid then appeared in the cytoplasm and increased enormously, producing the characteristic inclusion body which, it is suggested, probably consisted primarily of a mass of virus particles. The cytoplasmic trabeculae appeared to be cords of ribose nucleic acid compressed by the desoxyribose nucleic acid. Fully-formed, brick-shaped virus particles were plentiful in molluscum bodies. Only "less mature" forms had a marked granular structure. The virus particles appeared to consist of aggregations of smaller particles.

E. Lipman Cohen

**296. Failure of Adenosine-5-monophosphate to Affect Favorably Pruritus of Atopic Dermatitis**

A. ROSTENBERG, M. J. BRUNNER, and J. M. RIDDELL. *Journal of Investigative Dermatology [J. invest. Derm.]* **14**, 401-402, June, 1950. 2 refs.

Eight patients with moderately severe to severe atopic dermatitis were treated in hospital with 20 mg. adenosine phosphate hourly for 5 consecutive hours over a period of 3 days. The drug had no effect on the pruritus.

James Marshall

**297. Acute Disseminated Lupus Erythematosus. Report of a Case Treated with Adrenocorticotrophic Hormone (ACTH), with Clinical and Metabolic Observations and Autopsy Findings**

R. L. WHIPPLE and J. K. DAVIDSON. *Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.]* **36**, 206-217, Aug., 1950. 6 figs., 22 refs.

The authors report the case of a postmenopausal patient with disseminated lupus erythematosus, confirmed by biopsy, who was treated at the Emory University Hospital, Atlanta, Georgia, with adrenocorticotrophin (ACTH). The patient received 25 mg. of ACTH every

6 hours for 9 days, and then every 12 hours for 2 days. There was a dramatic transient clinical and haematological improvement, but the morphological condition and ultimate course of the disease were not changed by ACTH therapy. Detailed clinical, metabolic, and necropsy findings are presented [and should be consulted in the original by those interested].

N. R. W. Taylor

298. **Forty-four Cases of Lupus Erythematosus.** (Considerazioni su 44 casi di lupus eritematoso)

G. CALETTI and V. RESTA. *Dermosifilografico* [Dermosifilografico] 25, 261-281, May, 1950.

299. **Pityriasis Rubra Pilaris with Tumour Formation.** (Pityriasis rubra pilaire avec formes tumorales)

R. LAKAYE. *Archives Belges de Dermatologie et de Syphiligraphie* [Arch. belges Derm. Syph.] 13, 4-8, 1950. 2 figs., 4 refs.

The author reports a case of typical pityriasis rubra pilaris of the face in which there were numerous small sebaceous cysts and large elevated plaques. The histological picture was of a deep dense infiltration with numerous plasmocytes and histocytes, suggesting a malignant granulomatosis. The vitamin-A content of the blood was normal. The disease follows a chronic course and tends to clear up.

James Marshall

300. **On Impetigo Herpetiformis and its Connection with Parathyroprival Tetany.** [In English]

B. ENGFELDT and H. GENTLE. *Acta Dermato-Venereologica* [Acta derm.-venereol., Stockh.] 30, 50-57, 1950. 5 figs., 24 refs.

301. **The Response of the Sweat Glands to Some Locally Acting Agents in Human Subjects**

H. D. JANOWITZ and M. I. GROSSMAN. *Journal of Investigative Dermatology* [J. invest. Derm.] 14, 453-458, June, 1950. 1 fig., 19 refs.

Intracutaneous injection of the acetylcholinesterase inhibitors, neostigmine and physostigmine, induced sweating locally and potentiated the response to acetylcholine. Postganglionically denervated sweat glands, though not responding to local injection of a variety of parasympatheticomimetic drugs alone and in mixtures, responded to intense heat. Adrenaline, neostigmine, physostigmine, and histamine, when added to acetylcholine and injected, did not stimulate the denervated glands. The threshold dose of acetylcholine inducing sweating on local injection and axon-reflex sweating is higher for women than for men. The axon type of sweating response increased as the concentration of acetylcholine increased; high concentrations did not cause inhibition.

James Marshall

302. **Failure of Modern Footwear to Meet Body Requirements for Psychic and Thermal Sweating**

L. E. GAUL and G. B. UNDERWOOD. *Archives of Dermatology and Syphilology* [Arch. Derm. Syph., Chicago] 62, 33-45, July, 1950. 3 figs., 10 refs.

Effective aeration of the feet and the use of absorbent fibre in socks and shoes is important for the removal of

water vapour from sweat in the maintenance of foot hygiene. The temperature of the feet is important in the regulation of body temperature. Excessive moisture increases susceptibility to irritation and sensitization of the skin.

John T. Ingram

303. **Alopecia Areata. A Statistical Study and Consideration of Endocrine Influences**

S. A. WALKER and S. ROTHAM. *Journal of Investigative Dermatology* [J. invest. Derm.] 14, 403-413, June, 1950. 11 refs.

A statistical study was made of 230 cases of alopecia areata. In 84% of cases the condition developed before the age of 40. It occurred equally commonly in both sexes at all ages. Among 120 patients followed up for from 5 to 36 years, the initial attack lasted less than 6 months in one-third and less than one year in one-half. One-third did not recover from the attack during the whole period of observation.

Relapses occurred in 86% of the whole series and in 100% of patients followed up for 20 years or more. The course of the disease was most severe when it began before puberty. Some 75% of patients developing alopecia totalis remained totally bald for the period of observation.

The overwhelming majority of patients showed no evidence of endocrine abnormality. Certain observations made during the study suggest that endocrine factors may play an accessory or modifying part: (a) The course of disease is severest when it begins before puberty. (b) Some patients with alopecia totalis recover during pregnancy and lactation. (c) Some cases coincide in onset with development of thyrotoxicosis.

James Marshall

304. **Lesions of the Scalp in Certain Scaly Dermatoses. Histologic Study**

C. W. LAYMON. *Archives of Dermatology and Syphilology* [Arch. Derm. Syph., Chicago] 62, 181-191, Aug., 1950. 5 figs., 7 refs.

The differentiation of several scaling dermatoses is often very difficult clinically when the scalp alone is affected. In order to see whether these conditions could be differentiated histologically, biopsies were performed of the scalp lesions in 8 cases of circumscribed neurodermatitis (suboccipital dermatitis, lichen chronicus simplex), 13 cases of psoriasis, 14 of seborrhoeic dermatitis, 15 of chronic discoid lupus erythematosus, and 5 of lichen planus. It was found that with neurodermatitis, psoriasis, and seborrhoeic dermatitis, although in some cases the scalp showed features diagnostic of the condition similar to those occurring on the non-hairy skin, in others the histological picture did not permit a certain and positive differential diagnosis between these three conditions to be made. On the other hand in active lesions of lupus erythematosus and lichen planus the same characteristic pathological picture is seen in the scalp as in the non-hairy skin, so that in these conditions biopsy is of value diagnostically. Old inactive lesions of lupus erythematosus, however, do not show any characteristic change.

H. R. Vickers



## Venereal Diseases

### 305. Isolation of the *Treponema pallidum* from Three Patients with Visceral Syphilis by Means of Animal Inoculation

E. CALKINS, F. LONDON, S. M. MELLINKOFF, T. VAN METER, and T. B. TURNER. *Bulletin of the Johns Hopkins Hospital [Bull Johns Hopk. Hosp.]* 87, 61-73, July, 1950. 2 figs., 21 refs.

*Treponema pallidum* has rarely been isolated from the viscera of patients with late or latent syphilis, though isolation is easy in experimental animals. The authors report successful isolation from 3 patients. The first patient suffered from gummata of the liver, and a portion of a gumma excised at laparotomy was inoculated into the testicle of a rabbit, which developed syphilitic lesions after 5 to 7 days; these showed *Treponema pallidum* on dark-ground examination and the infection was successfully transferred to another animal. The second patient was suffering from florid secondary syphilis with hepatitis; a portion of the liver was proved by animal inoculation to contain *Treponema pallidum*, but the blood serum gave negative results on inoculation. The third patient was thought to be suffering from syphilis of the stomach; a portion of this organ appeared to be syphilitic on histological examination, but did not prove infective, because it had been treated with formalin; however, a lymph node from the gastro-colic ligament when emulsified and injected into a rabbit was proved to contain *Treponema pallidum*.

It is pointed out that spirochaetes have to be present in considerable numbers before they can be regularly demonstrated by dark-ground microscopy or tissue-section staining, but even as few as 10 or 20 are likely to produce infection in the rabbit. Suspected tissue should be emulsified and injected within 2 hours of removal from the patient into 2 rabbits (in case one dies), which should be kept at 68° F. (20° C.) or less over a period of not less than 90 days. It is suggested that this method of establishing the nature of syphilitic lesions should be more widely adopted.

T. E. Osmond

### 306. Treatment of Syphilis with Aureomycin. A Preliminary Report

S. OLANSKY, R. B. HOGAN, S. R. TAGGART, G. S. LANDMAN, and E. D. ROBIN. *American Journal of Syphilis, Gonorrhoea, and Venereal Diseases [Amer. J. Syph.]* 34, 436-442, Sept., 1950.

A preliminary report on the effect of treatment with aureomycin in 108 cases of syphilis indicates that the lesions of the primary and secondary stages heal as rapidly as with penicillin therapy. *Treponema pallidum* disappeared from the surface lesions in 23 to 30 hours; increasing the dosage did not shorten the time of disappearance.

After a preliminary trial (with poor results) of dosages ranging between 30 and 240 mg. per kg. body weight per day for 4 days or less, patients with early syphilis were

given either (a) 30 mg. per kg. daily for 4 or 8 days, or (b) 60 mg. per kg. daily for 8 days. After observation for periods up to 7 months, 1 out of 17 patients given the former dose for 8 days, and 1 out of 24 given the latter dose required re-treatment, for reinfection in both cases. (Only 11 of group (a) and 5 of group (b) had been observed longer than 6 months.) Treatment for shorter periods was less successful. In late cases nodular syphilides were noted to heal rapidly. In 7 patients with chancroid as well the lesions all healed within 4 days. Granuloma inguinale lesions present in 3 patients were completely healed at the end of the aureomycin course.

Among a total of 108 patients treated, reactions—most frequently gastro-intestinal—were noted in 46. The Jarisch-Herxheimer reaction occurred in 5 patients.

V. E. Lloyd

### 307. Oral Treatment of Neurosyphilis with Aureomycin

R. R. KIERLAND and P. A. O'LEARY. *American Journal of Syphilis, Gonorrhoea, and Venereal Diseases [Amer. J. Syph.]* 34, 443-452, Sept., 1950. 4 refs.

The effects of treatment with aureomycin in 12 cases of neurosyphilis (3 asymptomatic, 2 of meningovascular syphilis, and 7 of tabes or paresis) are recorded. The majority of the patients were given 60 to 67 g. of aureomycin orally (2 to 3 g. daily at 6-hourly intervals over a period of 20 to 28 days). Symptomatic improvement and increase in weight were noted in most of the parietic patients. In all cases the cell count in the cerebrospinal fluid was markedly decreased, and its content of protein was much diminished in all except one patient. The results of the Lange reaction and serological tests usually showed no change after observation periods varying from 113 to 258 days. The authors conclude that the early results achieved with aureomycin in neurosyphilis are equivalent to those achieved with penicillin.

V. E. Lloyd

### 308. Results of Single and Multiple Injection Schedules for the Treatment of Early Syphilis with Penicillin in Oil and Aluminum Monostearate

E. W. THOMAS, C. R. REIN, S. LANDY, and D. K. KITCHEN. *American Journal of Syphilis, Gonorrhoea and Venereal Diseases [Amer. J. Syph.]* 34, 331-337, July, 1950. 4 refs.

Of 71 patients with early syphilis (44 with secondary syphilis), 23 received a single injection of 2,400,000 units of procaine penicillin with aluminium monostearate (PAM) and 48 were given only 1,200,000 units. After a follow-up period of 6 to 20 months, 60 (84.5%) were serum-negative when last examined, 7 still had positive titres of 16 units or less in the Kahn test, 1 was being treated for serum-resistance, 2 had relapse-reinfections, and one had a definite reinfection. Of 67 patients with early syphilis (44 with secondary

syphilis) treated with 1,200,000 units of PAM once a week for 2 weeks and followed up for 6 to 20 months, 41 (61.2%) were serum-negative when last examined, 17 had Kahn titres of 16 units or less, 3 were re-treated for serum-resistance, 4 had relapse-reinfections, and 2 had definite reinfections. Of 68 other patients with early syphilis (30 with secondary syphilis) treated with 1,200,000 units of PAM once a week for 4 weeks and followed up for 6 to 20 months, 41 (60.3%) were serum-negative when last examined, 20 had Kahn titres of 16 units or less, 4 were re-treated for serum-resistance, and 3 had relapse-reinfections.

The re-treatment rates for the three groups were thus 5.7%, 13.4%, and 10.4% respectively. It is concluded that the results obtained by the single-injection method appear to be as good, after the period of follow-up stated, as those of any rapid treatment method previously tried at the Bellevue Hospital.

R. R. Willcox

309. The Antiluetic Properties of Tyrothricin and Streptomycin. [In English]

A. BESSEMAN and R. DEROM. *Antonie van Leeuwenhoek [Antonie v. Leeuwenhoek]* 16, 295-298, 1950. 7 refs.

310. A Proposal for Joint Action Against Congenital Syphilis

B. HUSE and W. H. AUFRANC. *Journal of Venereal Disease Information [J. vener. Dis. Inform.]* 31, 174-177, July, 1950. 1 ref.

311. Status of Treatment of Syphilitic Pregnant Women and of Children who Have Congenital Syphilis

M. S. GOODWIN. *Journal of Venereal Disease Information [J. vener. Dis. Inform.]* 31, 178-184, July, 1950. 26 refs.

312. The Morphology and Staining Characteristics of the *Treponema pallidum*. Review of the Literature and Description of a New Technique for Staining the Organism in Tissues

R. E. CAMPBELL and P. D. ROSAHN. *Yale Journal of Biology and Medicine [Yale J. Biol. Med.]* 22, 527-543, July, 1950. 8 figs., bibliography.

313. The Treatment of Gonorrhea in Women with Streptomycin

A. M. SALZBERG, C. W. CAULKINS, and R. H. HOGE. *American Journal of Obstetrics and Gynecology [Amer. J. Obstet. Gynec.]* 60, 217-220, July, 1950. 8 refs.

Streptomycin was given to 18 women, 16 of whom had acute pelvic gonorrhoea and 2 asymptomatic gonorrhoea. All but one were treated as out-patients with streptomycin, 750 mg. being injected intramuscularly each day for 3 successive days. One, an in-patient, was given the same daily dose for 6 days. Examinations, including study of cervical and urethral smears and erythrocyte sedimentation rate (E.S.R.), were repeated weekly for 3 weeks and then monthly for 3 months. Three consecutive negative smears constituted a "cure".

Before treatment, the majority of patients had severe low abdominal pain, pyrexia, and an average E.S.R. of 22.8 mm. in one hour. Nine patients had a palpable,

inflamed Fallopian tube. After treatment, pelvic tenderness decreased markedly within 24 hours, temperature becoming normal within 48 hours. The adnexal masses disappeared within 2 months in 5 cases, and were present, but smaller, in 3 cases after 3 months. The average E.S.R. was 15.3. Smears became negative within 24 hours in 7 cases, within 48 hours in 5 cases, and within the first week in 5 more cases. One patient developed perihepatitis, and a *Trichomonas vaginalis* infection in another was not altered by the streptomycin. Although 17 patients were cured, two courses of streptomycin failed to cure the eighteenth.

T. Anwyl-Davies

314. The Treatment of Gonococcal Arthritis with Streptomycin

H. L. HIRSH and W. KURLAND. *Medical Annals of the District of Columbia [Med. Ann. Distr. Columbia]* 19, 307-309, June, 1950. 3 figs., 5 refs.

315. Streptomycin Treatment of Granuloma Inguinale

H. PARISER, S. Z. GOLDBERG, and G. H. MITCHELL. *Archives of Dermatology and Syphilology [Arch. Derm. Syph., Chicago]* 62, 261-268, Aug., 1950. 5 refs.

The results are described of streptomycin treatment of 76 patients diagnosed as having granuloma inguinale by identification of intracellular Donovan bodies. All the patients received 3.6 g. per day for 5 days, that is, a total of 18 g. in individual doses of 0.6 g. every 4 hours day and night.

Failure was recorded if Donovan bodies were discovered in smears from the lesions after completion of the 5-day course of treatment (12 cases), or if the lesions recurred after healing completely (3 cases). These cases were all re-treated with 4 g. of streptomycin daily for 10 days in doses of 0.67 g. every 4 hours day and night. This second course raised the cure rate to 96%, for it was successful in 12 cases but 3 cases failed to respond. Over 60% of the patients were observed for longer than 6 months; the lesions of 61 (80%) healed with the initial course of streptomycin.

T. Anwyl-Davies

316. Aureomycin in the Treatment of Granuloma Inguinale and Lymphogranuloma Venereum

V. S. WAMMOCK, R. B. GREENBLATT, R. B. DIENST, C. CHEN, and R. M. WEST. *Journal of Investigative Dermatology [J. invest. Derm.]* 14, 427-434, June, 1950. 5 refs.

Oral (but not parenteral) administration of aureomycin is very effective in granuloma inguinale. The minimum effective dose appears to be 20 g. over 10 days, but prolonged therapy is necessary for patients with extensive lesions.

In lymphogranuloma venereum aureomycin was more valuable in late cases than in relatively early cases with buboes. Proctitis responded well. Daily manual dilatation of rectal strictures during aureomycin treatment gave good results and reduced the need for colostomy. Ulcerative lesions responded poorly. The minimum effective dose for buboes was 20 to 30 g. given in 0.5 g. doses four times daily; in cases of proctitis and stricture 40 to 80 g. or more was required.

James Marshall

## Genito-urinary Disorders

### 317. Studies on Nephrosis. Quantitative Changes in Enzymes of the Gastroduodenal Fluids

A. M. CARPENTER and M. L. MENTEN. *American Journal of Clinical Pathology* [Amer. J. clin. Path.] 20, 619-629, July, 1950. 1 fig., 19 refs.

The pH and enzyme content of saliva, gastric juice, and duodenal juice were studied in 10 patients with nephrosis, 9 patients with no gastro-intestinal disease, 6 patients with coeliac disease, 6 patients with cystic fibrosis of the pancreas, and 3 patients with glomerulonephritis. The patients with nephrosis were divided into three subgroups, the first containing 3 patients in whom the syndrome was believed to have resulted from sulphonamide administration, the second 5 patients with lipoid nephrosis, and the third 2 patients with features of nephrosis and nephritis.

Alterations in the secretions in nephrosis were of the same type as those occurring in children with coeliac disease or cystic fibrosis of the pancreas, whereas patients with nephritis excreted increased quantities of gastric fluid of low mucoid content. The possible role of the diminished enzyme secretion in the pathogenesis of the nephrosis is discussed.

[Whether sulphonamide administration played any part in the genesis of the nephrosis in the subgroup "sulpha nephrosis" seems doubtful.] G. M. Bull

### 318. The Relief of Nephrotic Edema by Dextran Infusions. [In English]

G. WALLENIUS. *Scandinavian Journal of Clinical and Laboratory Investigation* [Scand. J. clin. Lab. Invest.] 2, 228-238, 1950. 4 figs., 30 refs.

A solution of 10% "dextran" in 0.9% saline was administered to some patients with nephrosis, and dextran in water to others. A nephrotic 9-year-old boy was given 80 ml. of the former every few days. He lost 0.5 kg. of weight each time, and was much improved at the end. Three more cases, one with signs of nephritis and gross oedema and one with azotaemia, were also successfully treated as far as oedema was concerned. Presence of salt in the infusion appeared to make no difference. The mechanism of the action of dextran is discussed and many interesting points are brought out.

G. Loewi

### 319. The Effects of Concentrated Salt-poor Albumin on the Metabolism and Excretion of Water and Electrolytes in Nephrosis and Toxemia of Pregnancy

F. ORLOFF, L. G. WELT, and L. STOWE. *Journal of Clinical Investigation* [J. clin. Invest.] 29, 770-780, June, 1950. 5 figs., 38 refs.

The intravenous administration of 400 ml. of a solution containing 25 g. per 100 ml. of salt-poor albumin resulted in a diuresis of both water and salt in 3 patients with the nephrotic syndrome and in one patient with toxemia of pregnancy. In a further 2 patients suffering

from toxemia of pregnancy no diuresis of either water or salt occurred.

Observations on the blood volume, serum protein concentration, osmotic pressure of the protein, concentration of serum sodium, chloride, and potassium, rates of excretion of the same ions, and clearances of creatinine and urea were made. An interesting observation was that sodium diuresis resulted only when the sodium concentration in serum had become elevated because of water diuresis.

[The results of the treatment cannot be adequately summarized. Workers with special interests in sodium and water metabolism will find this paper of great interest.]

G. M. Bull

### 320. Treatment of Nephrosis with Concentrated Human Serum Albumin. II. Effects on Renal Function and on Excretion of Water and Some Electrolytes

J. A. LUETSCHER, A. D. HALL, and V. L. KREMER. *Journal of Clinical Investigation* [J. clin. Invest.] 29, 896-904, July, 1950. 4 figs., 32 refs.

To 13 adults with the characteristic features of the nephrotic syndrome but without significant hypertension or azotaemia the authors gave intravenous injections of 100 ml. of 25% albumin solution twice daily for 3 to 6 days. A careful check was kept on weight, diuresis, blood electrolyte concentration, and excretion for 1 to 2 weeks afterwards. [The clinical data were published in an earlier paper (J. clin. Invest., 1949, 28, 700: see Abstracts of World Medicine, 1950, 7, 195).] In 5 of the patients the oedema disappeared completely; the remaining 8 showed a sharp increase in diuresis during the first 24 hours of treatment and a gradual falling off during the following days, in spite of continued albumin injections.

The authors' observations were as follows: The excretion of electrolytes follows the volume of urine, except for sodium, the excretion of which is governed by different laws; it varies widely in the same patient on different days; one patient was given three courses of albumin injections, and the pattern of diuresis and sodium excretion was different on each occasion. [Nothing is stated about any simultaneous clinical changes.] Low glomerular filtration rate goes parallel with low sodium output and intractable oedema. The extent of endocrine control of tubular reabsorption and its effect on nephrotic oedema is problematical; protein deficiency, hypoproteinaemia, reduction in blood volume, and plasma sodium concentration have also to be considered, but at present their part, either single or combined, cannot be assessed with any certainty. Five factors are involved after albumin injections: increase in plasma osmotic pressure; dilution of plasma with extracellular fluid almost to the original plasma concentration; increase in glomerular filtration; increase in the excretion of water; and increase in serum sodium concentration. The authors see here two possibilities: (1) With adequate



glomerular filtration the tubules may reject some sodium; the amount of sodium excreted in the urine determines the subsequent diuresis and the increase in plasma protein concentration. (2) No sodium is excreted; in that case the increased concentration of serum sodium apparently stops the water diuresis. L. H. Worth

### 321. Puerperal Uraemia due to Acute Upper-nephron Nephrosis. Report of Three Cases

A. D. T. GOVAN and I. MACGILLIVRAY. *Lancet* [Lancet] 2, 128-133, July 22, 1950. 9 figs., 18 refs.

It has so far been assumed that puerperal uraemia is nearly always due to either bilateral renal cortical necrosis or lower-nephron nephrosis. In this article, the authors describe 3 cases associated with an acute lesion of the upper nephron. The first patient was a woman of 36 years who, after delivering herself of child after 35 weeks of pregnancy, continued to bleed and became shocked. In a few days she became jaundiced, the blood urea level gradually rose, and she eventually died. Post mortem, both the liver and kidneys were enlarged. Microscopically, the liver showed areas of necrosis, involving mainly the middle and central zones of the lobules; there was also interstitial oedema. In the kidneys the epithelium of Bowman's capsule was swollen and pale; the proximal convoluted tubules were very hydropic, with small dark nuclei; the distal tubules were dilated.

The second patient also lost a great deal of blood. Oliguria followed, the blood urea level rose, and she died. Microscopically, the liver showed changes similar to those in the other case. In the renal cortex there were wedge-shaped areas of necrosis; the proximal tubules showed hydropic changes, but the glomeruli were fairly normal. The third patient also had severe haemorrhage; there was anuria and considerable vomiting, but the blood pressure remained at about 125/70 mm. Hg. She had convulsions and died with a considerably raised blood urea level. The liver showed changes similar to those in the other 2 cases. In the kidneys, both the glomeruli and distal convoluted tubules were normal, but the proximal tubules were hydropic with pyknotic nuclei.

In 2 of the cases slight cortical necrosis was present, but the authors stress the clinical observation that in true cortical necrosis the patients remain relatively symptom-free until the late stages. Evidently similar clinical pictures to those described here may occur after operations on the biliary tract. It is probable that the hepatic necrosis occurs during the phase of low blood pressure. The renal changes are possibly due to metabolic changes. Bell has described similar changes after mismatched blood transfusions. Paul B. Woolley

### 322. Functional Changes in the Kidneys in Chronic Circulatory Insufficiency. (О функциональных изменениях почек при хронической недостаточности кровообращения)

S. G. VAJSBEJN. *Клиническая Медицина* [Klin. med., Mosk.] 28, No. 6, 45-52, June, 1950. 15 refs.

The author studied the renal function of 70 patients with severe decompensated circulatory insufficiency.

Of these, 51 had rheumatic valvular disease, 7 had cor pulmonale, 8 had coronary disease, and 4 had syphilitic mesaortitis. None of these patients gave any history of renal symptoms, and all had a normal or low arterial blood pressure. Twenty of the patients died while under observation. The tests used in measuring renal function included estimation of urea clearance and estimation of glomerular filtration by creatinine clearance.

It was found that chronic circulatory insufficiency reduced both glomerular filtration and tubular reabsorption, the former occurring sooner and to a greater degree than the latter, while the reabsorption of urea was diminished before that of water. The reduction in glomerular filtration leads to retention of urea, creatinine, and sodium chloride; the output of sodium chloride from the kidneys in circulatory failure is not related to the concentration of that salt in the blood. Urinary solutes are in low, relatively constant concentrations. There is usually no significant haematuria or albuminuria.

Jeffrey Boss

### 323. Changes in the Kidneys in Circulatory Insufficiency. (Изменения почек при недостаточности кровообращения)

L. S. SHVARTS and K. V. ISTOMINA. *Клиническая Медицина* [Klin. Med., Mosk.] 28, No. 6, 52-54, June, 1950.

In this short article some of the published work on haemo-renal indices in circulatory insufficiency is reviewed. In circulatory failure renal clearance is deficient only when renal involvement is severe. The greatest reductions in clearance are in patients with rheumatic glomerulonephritis, or with circulatory insufficiency accompanied by a recrudescence of the rheumatic process. The result of the Van Slyke test and Ambard's constant are more sensitive indices than is the glomerular filtration rate; it is desirable to estimate all the haemo-renal indices simultaneously. In the uraemic syndrome the clearance of the blood is most disturbed in cases in which the urine itself is abnormal and contains albumin, blood, or casts.

Jeffrey Boss

### 324. Diagnosis of Renal Stasis and its Role in Circulatory Insufficiency. (К вопросу о диагностике застойных почек и роли их в клинике недостаточности кровообращения)

N. J. CHERVJAKOVSKIJ. *Клиническая Медицина* [Klin. Med., Mosk.] 28, No. 6, 55-58, June, 1950.

In a series of 24 patients with cardiovascular disease the non-protein nitrogen concentration in the blood was estimated in all cases, the blood urea concentration in 20, and the blood amino-acid concentration in 14.

The figures for urea and amino-acids were all within normal limits, but 16 out of 24 patients had a blood urea concentration of over 45 mg. per 100 ml., the highest concentration being 75 mg. per 100 ml. Albuminuria was usually less than 5%, but a urinary protein concentration of 12% was found in one case.

The author points out that renal stagnation must be considered in accounting for the clinical picture in circulatory disease.

Jeffrey Boss

## Disorders of the Locomotor and Osseous Systems

325. "Nodular Fibrositic Fever", or the Syndrome of Acute Febrile Nodular Fibrositis. (Fiebre nodular fibrositica o síndrome de fibrositis nodular aguda febril) S. TARNOPOLSKY and A. COSTA. *Prensa Médica Argentina* [Prensa méd. Argent.] 37, 1640-1644, July 21, 1950. 7 figs., 7 refs.

The authors discuss the many names describing the condition of fibrositis, and consider it to be a chronic extra-articular form of rheumatism. They regard fever with fibrositis as very rare; one such case is described in detail, and photomicrographs are reproduced showing nodules with considerable leucocytic infiltration. The condition was characterized by fever, leucocytosis, moderate anaemia, and increase in the erythrocyte sedimentation rate. In the search for focal sepsis an apical abscess was found. The possibility of erythema nodosum was excluded.

Fibrositis secondary to arthritis, chickenpox, or other diseases is not difficult to explain, but the appearance of painful nodules in patients otherwise in perfect health is hard to account for. The appearance of such nodules, accompanied by fever and general malaise, has not been described before, although there are other recognized fibrositic conditions accompanied by fever, such as epidemic brachial neuritis and Bornholm disease.

The possible aetiology of the syndrome described is considered. It is proposed to call this condition provisionally "acute febrile nodular fibrositis" or "nodular fibrositic fever". The characteristic findings are: (a) an eruption of nodules, whose fibrositic character may be confirmed histologically, and (b) coincident signs and symptoms of infection. After the appearance of fever the nodules persist in some places and disappear in others. Considerable relief is obtained from administration of sulphur in oil.

René Méndez

326. The Morbid Physiology of Muscular Rheumatism. (Zur Pathophysiologie des Muskel-Rheumatismus) H. BAYER. *Zeitschrift für Rheumaforschung* [Z. Rheumaforsch.] 9, 210-223, Aug., 1950. 12 figs., 42 refs.

The author draws attention to the discrepancy in cases of muscular rheumatism between the clear-cut clinical findings of local nodular hardening and tenderness and the absence of any pathological changes in biopsy specimens. By means of the "musculometer" he attempted to show that the nodules are the result of physiological disturbance and are due to local tetanic contractions of muscle fibres.

The apparatus is designed to lead off by skin electrodes the action currents of underlying groups of muscle fibres and, after amplification, to record the "specific tone". The "specific tone" (Bayer and Ihlenfeldt, *Z. Kreislauf-Forsch.* 1950, 39, 289) is proportional to the product of the average frequency and the average amplitude of the action currents of the groups of fibres recorded, the

latter being itself proportional to the degree of muscle-fibre activity.

Results of this investigation in 3 cases are given; one was a case of lumbago and the other 2 were of spondylitis ankylopoietica, in all of which the "specific tone" was found to be raised over the palpable areas of hardening in the erector spinae muscles. Injection of 1% procaine solution reduced the "specific tone" and abolished the hardening at the site of the injection without affecting the normal increase in the "musculometer" reading on voluntary movement of the muscle.

The author concludes that the typical rheumatic nodules are the result of local tetany arising on the basis of the "idiomuscular reflex" of Hoffman (*Ergebn. Physiol.*, 1934, 36, 15), the sensitivity of which is heightened by the disease process, possibly as a result of local vascular disturbance. Procaine injection is known to affect the proprioceptive endings in muscle while leaving the motor end-plates almost uninfluenced (Bayer, *Klin. Wschr.*, 1949, 27, 122), thus breaking the reflex arc on the afferent side. The typical pain of muscular rheumatism is regarded as comparable with cramp and secondary to the long-sustained local tetanic contraction.

J. B. Stanton

327. The Sacro-iliac Joints in Ankylosing Spondylitis. (Les articulations sacro-iliaques dans la spondylarthrite ankylosante)

J. FORESTIER, J. ROTES-QUEROL, and F. JACQUELINE. *Revue du Rhumatisme* [Rev. Rhum.] 17, 407-448, Aug., 1950. 32 figs., bibliography.

### RHEUMATOID ARTHRITIS

328. Studies on the Effect of Neostigmine on Muscular Symptoms in Rheumatoid Arthritis. [In English]

T. WRAMNER. *Acta Medica Scandinavica* [Acta med. scand.] 138, Suppl. 242, 1-59, 1950. 17 figs., bibliography.

A syndrome comprising muscle pain, pain on motion, muscle tenderness to deep palpation, and decreased range of motion is common in rheumatoid arthritis. In this investigation possible causes of this syndrome and the effect of neostigmine are studied.

Thermo-electric recordings of the muscle temperature gave no support for the assumption that these symptoms are referable to any marked vasoconstriction in the muscles. The beneficial effect of neostigmine is probably not ascribable to any action on the vessels.

In electromyographic recordings from the affected muscles an involuntary activity in the voluntarily relaxed muscles was observed in 38 of 50 patients. In 36 of these 38 patients the electromyographic signs of muscle activity disappeared within 30 minutes after subcutaneous injection of 0.7 to 1.0 mg. neostigmine. Injection of

normal saline showed no effect on the activity. In 34 of the 38 patients with electromyographically demonstrable muscle activity the range of motion increased significantly after the injection of neostigmine. Electromyographic recordings of the patellar reflex showed that subcutaneous injection of a small dose (0.5 to 1.0 mg.) of neostigmine decreased while a large dose (1.4 to 2.0 mg.) of neostigmine increased the patellar reflex.

The present observations favour the theory that the discussed symptoms are caused by reflex contractions in the affected muscles and that neostigmine exerts its beneficial effect by an action on the spinal reflex arc. It is possible that those authors who found no beneficial effect of neostigmine therapy administered too large doses of neostigmine.—[Author's summary.]

**329. Disturbances of Sugar and Water Metabolism as an Expression of Diencephalic Disturbance in Rheumatoid Arthritis.** (Störungen des Wasser- und Zuckerstoffwechsels als Ausdruck einer diencephalen Störung bei chronischer Polyarthrit)

E. HILLER. *Zeitschrift für Klinische Medizin* [Z. klin. Med.] **146**, 569–577, 1950. 3 refs.

Studies of water and sugar metabolism in 40 cases of chronic rheumatoid arthritis showed disturbances in both these functions in almost all patients, suggesting that the pituitary–diencephalic apparatus is involved in this disease. This is further confirmed by the frequent occurrence of symptoms referable to the endocrine and vegetative nervous systems, which are closely connected with the diencephalic apparatus. The author believes that these disturbances are not the cause, but a secondary effect, of the rheumatic process. They are never found in cases of acute polyarthrit.

Marianna Clark

**330. Gold Therapy in Early Rheumatoid Arthritis**

C. H. ADAMS and R. L. CECIL. *Annals of Internal Medicine* [Ann. intern. Med.] **33**, 163–173, July, 1950. 12 refs.

An attempt was made to evaluate gold therapy in rheumatoid arthritis. The authors treated 106 early cases, and compared the results with those obtained in 83 controls treated by "conventional" methods. The standard of remission is not defined, but it was found that gold therapy resulted in more remissions more quickly than did the treatment given to the controls. The difference was less, however, when the two groups were assessed according to strict therapeutic criteria. [No mention is made of the method of selecting cases and controls, apart from the statement that in all the cases the disease was of less than one year's duration.]

D. P. Nicholson

**331. Pregnenolone in the Treatment of Rheumatoid Arthritis**

J. P. P. STOCK and E. C. McCCLURE. *Lancet* [Lancet] **2**, 125–128, July 22, 1950. 8 refs.

The authors investigated the effects of  $\Delta^5$ -pregnenolone acetate in oil in one case of ankylosing spondylitis and 9 cases of rheumatoid arthritis. The disease was clinically active and the erythrocyte sedimentation rate (E.S.R.)

raised in all. Patients were in hospital during the trial. Progress was assessed by estimations of the E.S.R. once or twice weekly, and weekly measurements of joint ranges, grip, and joint circumference. The drug was given intramuscularly, in daily doses of 200 mg. for 3 weeks. Control injections of oil were then given daily for 2 weeks and a second course of pregnenolone, combined with 1 g. ascorbic acid and 100 units hyaluronidase in the same syringe, was given for a further 2 weeks.

Of 10 cases treated, 3 showed measurable objective improvement. One of these was the case of spondylitis, in which improvement was continued for several months afterwards. It was therefore questionable whether it could be attributed to the drug. In one of the cases of rheumatoid arthritis improvement was already occurring before treatment and the condition did not relapse when the drug was withdrawn. In only one case could improvement be ascribed to pregnenolone. In this case the condition relapsed when the drug was withdrawn or when the dose was reduced. Joint effusions and the E.S.R. remained unchanged during the remission. In most of the cases subjective improvement was noted an hour or two after the injections, whether of pregnenolone or control oil.

Pregnenolone had no general toxic effects, but local reactions at the injection sites occurred in 7 cases and were severe in 5, preventing further administration in one. These local inflammatory injections (which might have been due to the solvent) were uninfluenced by the simultaneous injection of hyaluronidase.

Ellis Dresner

**332. The Effects of Adrenocorticotrophic Hormone (ACTH) in a Case of Juvenile Rheumatoid Arthritis**

P. ASTRUP, K. BRÖCHNER-MORTENSEN, V. FABER, C. HAMBURGER, N. HARBOE, K. SCHMITH, E. SNORRASON, M. SPRECHLER, and J. VESTERDAL. *Acta Paediatrica* [Acta Paediatr., Stockh.] **39**, 215–232, 1950. 8 figs., 19 refs.

The authors of this paper describe a case of rheumatoid arthritis treated with adrenocorticotrophin (ACTH). A 10-year-old girl had had rheumatic fever at the age of 1½ years. The heart was enlarged, but there was no electrocardiographic change. Following a recurrence at 2½ years she developed periodic attacks of febrile arthritis alternating with periods of comparative well-being. Three courses of gold treatment had little effect on the joints or the erythrocyte sedimentation rate (E.S.R.). The last febrile attack, in which pericarditis and anaemia developed, had started 6 weeks before the beginning of ACTH treatment, at which time she was emaciated (weight 17.8 kg., with normal height for her age), all joint movements were limited except at the toe and distal finger joints, there were contractures of the elbows, hips, and knees with atrophy of the muscles of the extremities, and she cried on the least passive movement. The lymph nodes were enlarged, but there was no splenomegaly. There was an apical systolic murmur and radiology showed enlargement of the heart.

At first she was given 25 mg. of ACTH daily in four intramuscular injections. Six hours after the first injection she could sit in a semi-erect position, the next day tenderness of the joints had gone, and after 3 weeks she



could ride a bicycle. Her appetite improved and she gained 2.4 kg. in weight in the first week. The dosage was gradually diminished by 8 or 10 mg. a day down to 4 mg. a day without recurrence. On the 21st day a cold caused fresh arthritis of the knees and elbows which disappeared after 4 daily doses of 4 mg. of ACTH. From the 26th to the 50th day of treatment she was given 2 mg. a day, whereupon the temperature rose and joint symptoms recurred. One week later she started a course of 25 mg. of ACTH daily for 4 days, followed by 5 mg. daily without improvement, and treatment was stopped on the 76th day after a total dosage of 572 mg. had been given.

Proteinuria (maximum excretion of 9 g. a day) developed on the 16th day of treatment and, in the absence of haematuria, hypertension, or rise in blood urea level, was diagnosed as due to nephrosis. The failure of the second course of treatment at high dosage to counter the relapse was possibly associated with the fact that the ACTH was of a different batch, and the authors, in an addendum, report a remission of joint symptoms and a fall in the E.S.R. after the administration of 50 mg. daily of yet another batch. After 3 days this course was stopped on account of increasing oedema. A Congo-red test showed 99% absorption of dye, indicating the presence of amyloidosis. During treatment the serum level of proteins (especially of the  $\alpha$ -globulins), uric acid, and non-specific hyaluronidase inhibitor decreased; there was no change in the electrolyte levels in the blood, but excretion results were inconclusive. The haemoglobin level, leucocyte count, and lymphocyte count increased and the eosinophil count decreased. In the first and third periods of high dosage, excretion of both 17-ketosteroids and glucocorticoids increased, while in the second period, when there was no clinical improvement, only the former increased. *A. W. Franklin*

**333. Apparent Free Histidine Plasma and Urine Values in Rheumatoid Arthritis Treated with Cortisone and ACTH** C. A. L. STEPHENS, E. B. WALLRAFF, A. L. BORDEN, E. C. BRODIE, W. P. HOLBROOK, D. F. HILL, L. J. KENT, and A. R. KEMMERER. *Proceedings of the Society for Experimental Biology and Medicine* [Proc. Soc. exp. Biol., N.Y.] **74**, 275-279, June, 1950. 2 figs., 9 refs.

A group of 15 patients with active rheumatoid arthritis were treated with cortisone or adrenocorticotrophin (ACTH) while under controlled conditions of metabolism, their urinary excretion and plasma level of histidine being measured. In 5 of these patients initial doses of 300 mg. of cortisone intramuscularly were followed by 100 mg. daily; 10 patients were given from 40 to 160 mg. of ACTH daily in divided doses at 6-hourly intervals. Rapid subjective and objective improvement occurred in all patients. Histidine was measured in the plasma and in 24-hour collections of urine by a microbiological technique, in which the test organism was *Leuconostoc mesenteroides* P-60. All specimens from each patient were assayed in one series and hydrous histidine hydrochloride was used as a standard. There was a striking increase in the excretion of apparent free histidine in the urine during treatment with both drugs. The plasma levels were not significantly altered, however,

although the maximum values reached during treatment showed a significant rise when compared with the highest control values. *A. C. Crooke*

**334. Desoxycorticosterone Acetate and Ascorbic Acid Injections in Rheumatoid Arthritis**

D. H. KLING. *Journal of the American Medical Association* [J. Amer. med. Ass.] **143**, 791-792, July 1, 1950. 8 refs.

The effect of the administration of 5 mg. of desoxycortone acetate by intramuscular injection followed by intravenous or intramuscular injection of 1,000 mg. of ascorbic acid has been studied in 14 cases of rheumatoid arthritis; 2 patients received daily injections, the rest were given injections two or three times weekly. Patients were advised to reduce salt intake during treatment.

In only 1 patient was there objective improvement; 1 was subjectively improved, 6 were unaffected, and 6 became worse, 5 of these last having acute exacerbations. One patient receiving daily injections developed hypertension with heart failure after the 13th injection. Another patient, who received injections every 3rd day, developed hypertension after the 6th injection. One patient given daily injections developed, after some 2 weeks' treatment, greatly increased weakness and soreness of the muscles, ascribed to a low serum potassium level. *Kenneth Stone*

**335. The Treatment of Chronic Joint Diseases with Combined Injections of Deoxycortone and Ascorbic Acid.**

(Die Behandlung chronischer Gelenkerkrankungen mit kombinierten Injektionen von DOCA-Ascorbinsäure) J. WITZGALL. *Therapie der Gegenwart* [Ther. d. Gegenw.] **89**, 258-262, Aug., 1950. 3 refs.

**336. Effects of Compound E in Three Cases of Rheumatoid Arthritis.** (Effets du complexe adrénocortical E dans 3 cas de polyarthrite chronique évolutive)

J. FORESTIER, A. CERTONCINY, F. JACQUELINE, and F. GERBAY. *Bulletin de l'Académie Nationale de Médecine* [Bull. Acad. nat. Méd., Paris.] **114**, 489-494, July 11, 1950. 3 figs.

## BONE DISEASES

**337. Internal Frontal Hyperostosis.** (Zgrubienie kości czołowej (hyperostosis frontalis interna))

G. FIAŁKOWSKI. *Polski Tygodnik Lekarski* [Polsk. Tyg. lek.] **5**, 817-821 and 856-867, May 22 and 30, 1950. 12 figs., 35 refs.

This detailed survey of the literature dealing with internal frontal hyperostosis is followed by a description of 6 cases (in females). These were found by a study of 4,000 x-ray films of the cranium. Hyperostosis of the frontal bone was associated with signs indicating pituitary dysfunction. Obesity, virilism, headaches, and insomnia were present in all cases. Two of the patients suffered from mild diabetes. There was a close resemblance to the Stewart-Morel syndrome but no evidence of Cushing's disease. The changes in the skull could not be related

to senility, for the age of patients varied from 19 to 68 years. The relation of this syndrome to acromegaly and metabolic craniopathy is discussed.

J. T. Leyberg

338. **A Disturbance of Bone Growth: Epiphyseal Dysgenesis in Athyroidism and Hypothyroidism.** (Una particolare turba dell'accrescimento osseo: la disgenesia epifisaria nell'atireosi e nell'ipotireosi) C. LOMBROSO. *Minerva Pediatrica* [Minerva Pediat.] 2, 328-340, July, 1950. 19 figs.

The clinical and radiological features of epiphyseal dysgenesis are discussed with reference to 10 patients, diagnosed by the author as suffering from congenital or acquired hypothyroidism, in all of whom punctate dysgenesis was demonstrable in various epiphyses and bones (including the spine, the ischio-pubic junction, and the trapezium) and responded fairly rapidly to thyroid medication. The author discusses briefly the differential diagnosis, mainly from the various forms of osteochondritis, and stresses the need for repeated radiological examination of the whole skeleton, even after beginning treatment, if bony changes are to be detected and controlled in cases of thyroid deficiency.

P. E. Polani

339. **Bony Tumours in Paget's Disease.** (Les tumeurs osseuses de Paget)

L. CORNIL, J. PAOLI, H. GASTAUT, and H. SPITALIER. *Semaine des Hôpitaux de Paris* [Sem. Hôp. Paris] 26, 2347-2361, July 2, 1950. 7 figs., bibliography.

Four cases of Paget's disease, with a total of ten tumours, are reported. Among these, three types of benign tumour were noted [an observation stated by the authors to be original]. These types are named: (a) simple fibroma; (b) simple or metaplastic histiocytoma; (c) hypertrophic giant-cell histiocytoma. The malignant tumours described are: (a) polymorphic reticulosarcoma; (b) reticulosarcoma with myeloplasia; in none of these cases were visceral metastases present, but all ended fatally.

The conclusion drawn is that the tumours arising in this condition are poorly differentiated connective-tissue tumours, and may be benign or malignant. They may arise in local or generalized forms of the disease, and may be the first feature to draw attention to the underlying disease. [Good photomicrographs are presented. The radiographic diagnosis is only briefly discussed.]

Donald McDonald

340. **Eosinophilic Granuloma. An Unusual Case with Involvement of the Skin, Lungs and Kidneys**

P. ADAMS and J. E. KRAUS. *Archives of Dermatology and Syphilology* [Arch. Derm. Syph., Chicago] 61, 957-970, June, 1950. 6 figs., 14 refs.

An extensive review of the literature "illustrates why the various attempts to classify the eosinophilic granulomas have so far been unsatisfactory". A very full report of the clinical course and of post-mortem findings in a case treated by the authors is given, illustrated with a photograph and photomicrographs and followed by a closely argued commentary.

[This paper needs to be read in full, as no satisfactory abstract could be made which would do it justice.]

J. E. M. Wigley

341. **Pseudocystic Disease of Bone**

W. E. JACOBSON. *Archives of Internal Medicine* [Arch. intern. Med.] 86, 35-50, July, 1950. 10 figs., 19 refs.

As clinical and radiological examination may fail to differentiate the bone lesions due to eosinophilic granuloma from those due to either lipid granulomatosis or fibrous dysplasia, it is suggested that the term "pseudocystic disease of bone" should be applied to all three conditions. Apparently the basic pathological process is a proliferation of the cells of the reticulo-endothelial system. Variants of the disease are represented by the syndromes of Albright and of Hand and Christian.

As regards the histological appearances which may be observed in pseudocystic disease, it is of interest to refer to the work of Green and Farber (*J. Bone Jt Surg.*, 1942, 24, 499). These investigators believe that eosinophilic granuloma constitutes the early phase of the disease, a phase in which bone destruction is associated with an infiltration with eosinophil and large mononuclear cells. Subsequently the eosinophil cell is no longer to be found and there is a predominance of vacuolated mononuclear cells. A fibroblastic ingrowth also occurs. The vacuoles become enlarged and foam cells are formed. The presence of fibrous connective tissue characterizes the final phase.

Four cases are described, in order to demonstrate the relation between the various conditions. The patients were men and their ages ranged from 22 to 53 years. The first patient was considered to be suffering from osteomyelitis of the mandible and diabetes insipidus. An area of rarefaction was observed on radiological examination of the mandible. Material obtained from the bone showed evidence of eosinophilic granuloma. Eventually a skiagram of the skull revealed multiple defects in the occipital region. Fibrous tissue and bone fragments were detected on histological examination of one of these lesions. In the remaining cases, defects were detected in the skull, in the pelvis, and in various long bones. One patient was found to have a lesion in the proximal phalanx of the right big toe. A specimen was removed from the bone; it contained hyaline cartilage. The findings were consistent with a diagnosis of fibrous dysplasia with cartilaginous metaplasia.

A. Garland

342. **Report of Two Additional Cases and an Analysis of the Pathogenesis of Ainhum on the Isthmus of Panama**

W. C. BUTZ and N. W. ELTON. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [Trans. R. Soc. trop. Med. Hyg.] 44, 113-116, July, 1950. 6 figs., 13 refs.

This is a well illustrated report of 2 cases of ainhum in elderly male negro labourers in the Panama Canal Zone. The condition was unilateral. Shoes had been worn during working hours. No new aetiological facts were discovered. The possibility of a familial trait subserving the purpose of biological elimination of a vestigial structure is suggested.

Clement Chesterman

# Neurology

## 343. Treatment of Neuronitis with BAL

J. M. NIELSEN. *Bulletin of the Los Angeles Neurological Society [Bull. Los Angeles neurol. Soc.]* 15, 61-71, June, 1950. 4 refs.

It was decided to treat "all cases of so-called neuronitis (polyneuritis with facial diplegia, infectious neuronitis, or the Guillain-Barré syndrome) with BAL [British antilewisite]". Ten cases so treated are described. It is said that in 9 cases benefit was obtained.

[The theoretical basis for the use of BAL in the Guillain-Barré syndrome is, to say the least, questionable. Still more so is the selection of cases. Of the 10 cases, one previously diagnosed as a case of muscular dystrophy was not admitted to hospital until 7 months after the onset of symptoms and was not improving until a year later. Others included cases of diphtheritic polyneuritis, polyneuritis complicating gold treatment, and diabetic neuropathy. In one case the protein content of the cerebrospinal fluid was normal, and it would seem that 6 of the 10 cases were almost certainly not examples of this syndrome. It is suggested that the syndrome is occasionally associated with porphyrinuria and that aneurin produces beneficial effects in "infectious polyneuritis"; neither of these statements will be universally accepted. Some of the clinical descriptions are equivocal, for example, "the umbilicus rising on testing", "the eye movements were grossly normal", "the eye grounds show no clear cut intracranial pressure", "all deep reflexes were absent but no pathologic reflexes were found", "examination showed all the cranial nerves to be negative, including the pupils".

No case has been made out in this paper for the statement that BAL has any action on the syndrome originally described by Guillain, Barré, and Gordon Holmes.]

Hugh Garland

## 344. Muscle Weakness and Wasting in Sciatica due to Fourth Lumbar or Lumbosacral Disc Herniations

E. KUGELBERG and I. PETERSÉN. *Journal of Neurosurgery [J. Neurosurg.]* 7, 270-277, May, 1950. 4 figs., 15 refs.

The authors have investigated 66 cases of muscle weakness or wasting due to fourth lumbar or lumbosacral intervertebral disk herniation at the Serafimer-lasarett, Stockholm. The cases discussed are those in which the diagnosis of disk herniation was subsequently confirmed at operation. Investigation was confined entirely to a study of motor changes, and care was taken to allow for functional paresis due to pain. Clinical and electromyographic examinations were carried out on the musculature of the lower leg and foot by the current methods of investigation (Kugelberg, *J. Neurol. Neurosurg. Psychiat.*, 1947, 10, 122). Of the 41 proven cases of fourth lumbar disk herniation, 37 showed muscular disturbance of some sort; this took the form of atrophy in 23, and a palpably soft consistency on maximal contraction of the extensor digitorum brevis in 12; 19

showed weakness of extensor hallucis longus, 17 weakness of the tibialis anterior, and 8 weakness of foot pronation. Of the 25 proven cases of lumbo-sacral disk herniation, there was muscular disturbance only in 4—weakness and wasting of the extensor group in 2, and the flexor group in 2. The findings indicate that the principal nerve supply of the extensor digitorum brevis is derived from the L5 segment, and the authors suggest that the constant involvement of this muscle in lesions of the fifth lumbar nerve root is due either to less segmental overlap in the innervation of the distal part of the limb than the proximal, or to the greater vulnerability of the longer nerve fibres compared with the shorter ones. The frequency of the affection of extensor digitorum brevis in fourth lumbar disk herniation is stressed.

Kenneth Tyler

## 345. The Use of 3-Methyl-5-phenylhydantoin (AC 114) in the Treatment of Epilepsy

S. LIVINGSTON and A. Y. SWEET. *Bulletin of the Johns Hopkins Hospital [Bull. Johns Hopk. Hosp.]* 86, 359-363, June, 1950. 1 ref.

At the epilepsy clinic of Johns Hopkins Hospital 42 patients were treated with "AC 114"; among them were 35 cases of idiopathic epilepsy and 7 of symptomatic epilepsy; 23 had grand mal, 7 had petit mal, 5 had psychomotor epilepsy, and 7 had grand mal mixed with petit mal or psychomotor epilepsy. In the whole group, 27 of the patients were given the drug in addition to their usual medication, which had proved ineffective; 15 had not previously received medication regularly and were given AC 114 alone. The patients were observed for from 3 to 12 months, and the number of fits while they were taking AC 114 was compared with that during an equal period immediately preceding the test. Of the 42 patients treated, fits were controlled in 14; in 9 the condition improved to the extent that only one-fourth of the previous number of seizures occurred; 2 patients had between one-half and one-fourth of the previous number, and in 17 the number of seizures was not reduced. The drug proved effective only in controlling grand mal. Of 23 cases of grand mal, only 3 were not improved, and 5 out of 7 patients with mixed attacks were relieved of the grand-mal component. Dosage varied from 0.3 g. in children to 1.0 g. in adults per day. There were side-effects in 2 cases only; in one, appearance of a rash and fever required cessation of the treatment after 10 days, while the other had a rash which did not reappear on a second trial of the drug. There was no evidence of ataxia, diplopia, gingival hypertrophy, drowsiness, or haematological or urinary changes with the doses employed in this series.

J. B. Stanton

## 346. Dystonia Musculorum Deformans, with Report of a Case in a Child

D. C. RYAN. *Medical Journal of Australia [Med. J. Aust.]* 2, 360-362, Sept. 2, 1950. 4 figs., 10 refs.



## ELECTROENCEPHALOGRAPHY

## 347. The Relation of Dehydration of the Brain to the Spreading Depression of Leão

W. H. MARSHALL. *Electroencephalography and Clinical Neurophysiology* [Electroenceph. & clin. Neurophysiol.] 2, 177-185, May, 1950. 4 figs., 26 refs.

It is suggested that a causal factor in the production of the slowly spreading waves of depression of cortical activity described by Leão (*J. Neurophysiol.*, 1944, 7, 359) is dehydration of the exposed brain of the experimental subject. In order to test this proposition the author has taken every precaution to avoid drying, the exposed brain being covered by a pool of paraffin during the greater part of the experiment.

No spreading depression was observed in records from the brains of 3 control cats during periods ranging from 4 to 9 hours, or of the experimental group of 20 cats during a preliminary period ranging from 80 minutes to 6 hours, except in one case on one occasion when the brain had been accidentally damaged. These 20 cats were then given 12 to 30 ml. of 90% sucrose per kg. body weight intravenously at a rate of 1 to 2.5 ml. per minute. Considerable shrinkage of the brain was achieved, but at the expense of great systemic strain which resulted in the death of 8 of the cats before shrinkage was considered sufficient. Definite spreading depression occurred in 11 of the remaining 12 cats. Attempts to rehydrate 6 of the animals resulted in further circulatory stress and were successful only in one case, in which spreading depression ceased.

[The evidence is accumulating that spreading depression is an experimental artefact. The author incidentally adds support to the view of Sloan and Jasper (*Electroenceph. & clin. Neurophysiol.*, 1950, 2, 59; *Abstracts of World Medicine*, 1950, 8, 301) that it is the basis of the phenomena observed on stimulating the so-called "suppressor areas".]

W. A. Cobb

## 348. The Electroencephalographic Changes after Hemispherectomy in Man

C. MARSHALL and A. E. WALKER. *Electroencephalography and Clinical Neurophysiology* [Electroenceph. & clin. Neurophysiol.] 2, 147-156, May, 1950. 8 figs., 1 ref.

The case histories of 4 patients are presented, 3 suffering from tumour of the right hemisphere and the fourth from a right traumatic encephalopathy, all of whom were treated by hemispherectomy, which was complete in 2 cases, a small part of the frontal lobe being left in the other 2. The pre-operative electroencephalogram in every case showed right-sided slow activity. After operation, activity from both sides was of lower voltage than before, but the alpha-rhythm was still present on the side of the absent hemisphere and, in 2 cases, was at times clearer than on the intact side. Similarly when seizure discharges were recorded from the patient with traumatic encephalopathy they were equally clear on the two sides except in the right temporal region, where the voltage was lower. Furthermore, in one of 2 patients who were subjected to photic stimulation the response

was clearer on the side from which the hemisphere had been removed.

[Similar unexpected findings were reported by Krynauw in 1949 to the Summer Meeting of the Society of British Neurological Surgeons, and have been confirmed by the abstracter.]

W. A. Cobb

## 349. Electroencephalography in a Series of 38 Tumours of the Posterior Fossa. (L'électroencéphalographie dans une série de trente-huit tumeurs de la fosse postérieure)

G. C. LAIRY-BOUNES and H. FISCHGOLD. *Semaine des Hôpitaux de Paris* [Sem. Hôp. Paris] 26, 2633-2635, July 22, 1950. 2 figs., 6 refs.

Out of 38 cases of posterior-fossa tumour, the electroencephalogram (EEG) in 22 was normal or borderline; in 10 it was moderately abnormal and only in 6 grossly so. All except one of these last patients were young subjects. A correlation was noted between the rate of tumour growth and EEG abnormality; in particular, the patients with tumours of the cerebello-pontine angle had a normal EEG [Hill and Parr, *Electroencephalography*, London, 1950]; on the other hand, surprisingly, so did 3 patients with acute non-encapsulated abscesses.

The EEG is not of much value in location of these tumours, but the association of severe papilloedema with a more or less normal EEG is very suggestive. Gross EEG changes are an indication for immediate operation.

W. A. Cobb

## CENTRAL NERVOUS SYSTEM

## 350. Periodic Alternating Nystagmus in Friedrich's Ataxia

W. F. GORMAN and S. BROCK. *American Journal of Ophthalmology* [Amer. J. Ophthal.] 33, 860-864, June, 1950. 8 refs.

Periodic alternating nystagmus, previously described in the literature in association with vestibular, cochlear, or cerebellar disease, has been observed in a patient with Friedrich's ataxia. Nystagmus, present in this case in positions of lateral and vertical gaze, was seen also in the primary position. Here a series of nystagmoid jerks, lasting about a minute, occurred first toward one side and then, after a few seconds' interval of mid-line standstill, toward the opposite side. These cycles were spontaneous, but could be augmented by vigorous head shaking and were found to continue regularly over a period of observation of some months.

H. E. Hobbs

## 351. Retrobulbar Neuritis and Disseminated Sclerosis. (Neuritis retrobulbaris og dissemineret sclerose)

K. HYLLESTED. *Ugeskrift for Læger* [Ugeskr. Læg.] 112, 853-865, June 15, 1950. 10 figs., 30 refs.

The author reviewed 96 cases of acute retrobulbar or optic neuritis in patients who had been admitted to the Kommunehospital, Copenhagen, between 1914 and 1938, a period ranging from 9 to 25 years having elapsed since the onset of ocular symptoms. Of the 96 patients 15 had died and 14 others could not be examined, but

were sent a questionnaire. In 67 cases a full neurological examination was carried out, with perimetry and scotometry. Females predominated, the proportion of women to men (65 to 31) being higher than in the total admissions to hospital. Only one of the women was pregnant when the retrobulbar neuritis developed. The peak incidence of retrobulbar neuritis in cases of disseminated sclerosis was between the ages of 25 and 35, whereas in cases due to other causes there were two peaks, at 30 and 50 respectively.

The neuritis was intrabulbar in 39 cases. Of the whole group, permanent scotomata occurred in 44% and visual acuity was depressed below 6/18 in 19%. The prognosis for vision was worse if the lesion affected extramacular fibres as well as the papillomacular bundle. Of patients with central scotomata, only in 12% was visual acuity later below 6/18, as opposed to 26% of those who had large scotomata breaking through to the periphery, or amaurosis. Temporal pallor was more commonly found after retrobulbar than after intrabulbar neuritis. Only 2 of the patients had signs of disseminated sclerosis when first admitted, whereas approximately one-third of the patients reviewed had frank disseminated sclerosis; another third had minimal neurological signs but were symptom-free, while the remainder showed no evidence of the disease. There was no evidence that the occurrence of optic neuritis in cases of disseminated sclerosis made the prognosis worse. Of 52 patients who, at the time of developing retrobulbar neuritis, had neither signs of the disease nor any symptoms suggestive of it, 33 remained free, 12 were found to have minimal neurological signs but no symptoms, and 7 had developed florid evidence of the disease. Of the whole group, 4 had died, 12 were invalids, and 14 were unfit for work as a result of disseminated sclerosis, 4 of the last group being incapacitated by visual defect.

In conclusion, the author remarks that if local disease can be excluded in a case of unilateral retrobulbar neuritis, and intoxication in a bilateral affection, the probability is very high that the cause is disseminated sclerosis.

John Foley

### 352. New Therapeutic Trials in Disseminated Sclerosis.

(A sclerosis multiplex néhány újabb kezelési kísérletéről) Z. BÖSZÖRMENYI. *Orvosi Hetilap* [*Orvosi Hetil.*] 91, 345-348, March 12, 1950.

The author studied the effect of various drugs in disseminated sclerosis at the Neurological Clinic of Budapest University. Dicoumarol was given to 36 patients, for 3 to 12 weeks, in daily doses of 50 to 180 mg. Prothrombin time was held at the level of 30 to 40 seconds and was determined by the one-stage method of Quick, modified by Horn. [Details of the modification are not given.] In 10 cases moderate improvement was observed, and questionable improvement in 7 cases; 14 cases remained unchanged and in 5 cases definite deterioration took place. In 2 cases transient haematuria was observed. The 5 cases of deterioration suggest that dicoumarol might even be dangerous, especially in the presence of bulbopontine foci, as demonstrated in the case of a 28-year-old woman who developed a condition resembling decerebrate rigidity and bulbar symptoms under treatment.

The effect of cerebrospinal fluid from patients with disseminated sclerosis on a thrombin-inactivator system was examined by the method of Gerendas. Acceleration of inactivation was observed, showing that the cerebrospinal fluid did not contain coagulation-stimulating lipoproteins in significant quantities. The author concludes that the slowing effect on thrombin inactivation, observed by different authors in disseminated sclerosis, is doubtful; this and his clinical observations on dicoumarol do not justify the administration of the drug in disseminated sclerosis.

"Mephenesin" was given as "symptomatic" treatment to 10 patients by intravenous or intramuscular injection of 10 ml. of solution every 2 or 3 days, 8 to 12 injections being given altogether. No toxic effects were observed. For 5 to 15 minutes after intravenous injection the drug produced a marked euphoric effect. In 2 patients this was followed by disturbances of perception. Vegetative symptoms (erythema, excessive sweating, dermatographism) were common. In some patients miosis was seen, and in 1 patient mydriasis. In 3 patients intense nystagmus persisted for half an hour. Muscle tonus decreased one minute after the injection, mainly in the spastic muscles. In some cases transient paresis occurred. The spasticity ceased for about  $\frac{1}{2}$  to 1 hour. In about half of the cases reflexes became exaggerated; in one case new pathological reflexes appeared. In the paretic cases reflexes became sluggish. Hyperalgesia was seen in 2 cases. In the author's view, the related symptoms show that mephenesin affects not only the spinal centres or peripheral nerves, but also the cerebrum. When the drug was given intramuscularly it produced a less marked but longer-lasting effect.

"Parpanit" was given to 5 patients. Because in 2 patients giddiness, palpitations, and even collapse appeared with larger doses, a dose of 4 tablets (each of 6.25 mg.) three times a day was given for 2 to 6 months. The clinical picture did not change significantly, but spasticity generally decreased, intention tremor slightly diminished, and there was a marked euphorizing effect, possibly due to the presence of subclinical frontomesencephalic foci. The area affected by parpanit may be located in the reticular substance of the midbrain.

Catherine Schöpfli

353. Late Results of Treatment of Disseminated Sclerosis and Acute Disseminated Encephalomyelitis with Specific Vaccine. (Отдаленные результаты лечения больных множественным склерозом и острым рассеянным энцефаломиелитом специфической вакциной)

M. S. MARGULIS. *Клиническая Медицина* [*Klin. Med., Mosk.*] 28, No. 6, 30-33, June, 1950.

### 354. Localization of Cord Tumours by Electromyography

P. F. A. HOEFER and S. M. COHEN. *Journal of Neurosurgery* [*J. Neurosurg.*] 7, 219-226, May, 1950. 15 refs.

An investigation of the value of clinical electromyography as a means of localization of tumours of the spinal cord in 88 cases was carried out by the authors at Columbia University and the Neurological Institute,

New York. The authors based their investigation on the fact that resting normal skeletal muscle shows no electrical activity, and that spontaneous electrical activity is indicative of irritative or degenerative changes in the afferent nerve supply. They used concentric needle electrodes and a six-channel Grass ink-writing oscillograph, with the amplifier gain regulated to give a deflection of 10 mm. with an input potential change of 100  $\mu$ V. Care was always taken to ensure complete relaxation of the subject in a comfortable position to avoid artefacts due to spastic posture, incomplete relaxation, or movement. Sedation or local analgesia was deemed unnecessary. Their findings with electromyography as a localizing agent are compared with those obtained from a study of motor signs alone or sensory level alone, or from radiological investigation alone. Electromyography gave a correct result in 83% of cases, motor-level study in 50%, sensory-level study in 67%, and radiology in 45%.

All the lesions investigated were subsequently verified by operation, necropsy, or unequivocally abnormal radiological findings. The authors state that they are unable to distinguish electromyographically between cases of root compression and of degeneration of anterior horn cells causing spontaneous electrical activity in resting muscle, apart from the diffuse activity present in the latter. They conclude that electromyography constituted the most accurate individual method of localization of cord lesions in their group of cases.

Kenneth Tyler

355. **A Comparison between the Voluntary and Electrical Activation of Motor Units in Anterior Horn Cell Diseases**  
E. KUGELBERG and D. TAVENER. *Electroencephalography and Clinical Neurophysiology* [Electroenceph. & clin. Neurophysiol.] 2, 125-132, May, 1950. 6 figs., 22 refs.

Buchthal and others have described synchronization of the motor-unit action potentials recorded from two or more needle electrodes inserted in the same muscle as being typical of anterior-horn-cell disease. The authors accept the observation as substantially correct, but doubt the explanation which has been put forward to account for the synchronization, namely, that there is interaction between the injured anterior horn cells.

The voluntary discharge from partially denervated muscles in 18 patients suffering from poliomyelitis, amyotrophic lateral sclerosis, or syringomyelia was compared with the discharge in response to stimulation of the nerve to the muscle by slowly rising current, the position of the recording electrode being the same in each case. It was not possible to distinguish between the two responses. Moreover, in the 11 cases in which synchronization was observed on voluntary contraction it was also present when the nerve was stimulated electrically. Evidence is offered which shows that this could not be a reflex response and consequently, if true synchronization be present, it must occur in the nerve or more peripherally. Neither the muscle nor the nerve has been found to be unduly irritable but rather the contrary, and the threshold for stimulation of the nerve

is pathologically high in cases of this type. The authors therefore regard it as most probable that apparent synchronization is due to recording from different parts of the same large motor unit.  
W. A. Cobb

See also Section Cardiovascular Disorders, Abstract 210.

## BRAIN

356. **Normal Mentality associated with a Maldeveloped "Rhinocephalon"**

P. W. NATHAN and M. C. SMITH. *Journal of Neurology, Neurosurgery and Psychiatry* [J. Neurol. Neurosurg. Psychiat.] 13, 191-197, Aug., 1950. 6 figs., 10 refs.

The brain is described of a man who died from chondrosarcoma of the ilium. No abnormalities in his mental state or nervous system had been detected during life in spite of very extensive clinical study; in particular, his sense of smell was normal. However, when his brain was examined several anomalies were observed. No striking abnormality was visible on the dorsal and lateral surfaces, but when the hemispheres were drawn apart it was seen that the gyri cinguli and corpus callosum were replaced by an irregular mass of white matter covered by transversely-running gyri, with several masses of ectopic grey matter on the under surface, which was partly adherent to the thalamus. Fimbria, fornix, and septum pellucidum were entirely absent. The poorly developed hippocampus and dentate gyrus were displaced caudally, lying completely posterior to the rather unusually extensive amygdaloid complex, and were continuous with their fellows across the midline. Their broad posterior continuation represented the isthmus of the gyrus fornicatus. The hippocampal gyrus was grossly underdeveloped and the hippocampal fissure absent, so that the hippocampus and dentate gyrus were visible from the ventral surface of the brain. The olfactory tract and mammillary bodies were normal.

Microscopically, the component cells of the hippocampal complex were normal, although reduced in number, the extensive amygdaloid complex having apparently increased spacing of cells, but not their number. Those structures normally receiving afferent fibres from the fornix were found to be normal except for some sparseness of cells in the tuber nuclei. All the thalamic nuclei and the corpus striatum were normal.

The authors discuss the absence of any obvious efferent pathway from the diminished hippocampus and the possible significance of this patient's normal control and expression of emotion, with reference to Papez's theory of the function of the gyrus fornicatus.

J. B. Stanton

357. **Athetosis and the Basal Ganglia. Review of the Literature and Study of Forty-two Cases**

M. B. CARPENTER. *Archives of Neurology and Psychiatry* [Arch. Neurol. Psychiat., Chicago] 63, 875-901, June, 1950. Bibliography.

The author has studied the literature of athetosis and, in particular, reports of the pathological findings at necropsy in 42 patients who suffered from this type of



involuntary movement, which can be differentiated readily from chorea. Hemiatetosis usually develops after hemiparesis or in association with it, the common cause being a necrotizing vascular lesion which destroys part of the internal capsule and the corpus striatum on the opposite side of the brain. Bilateral athetosis usually dates from infancy and in about half the cases is accompanied by bilateral paresis and spasticity. In about 80% of cases there is dysarthria, and in 58% mental deficiency.

The commonest pathological finding is bilateral status marmoratus in the corpus striatum, while in a smaller proportion of cases there is a bilateral vascular lesion in the same area. Rarely, no pathological lesion can be found in the corpus striatum in cases of double athetosis.

J. W. Aldren Turner

**358. Hepatolenticular Degeneration. Analysis of Dyskinetic Phenomena; Relation of Degree of Hepatic Damage to Course of the Disease; Nervous Disorders in Ordinary Disease of the Liver**

E. HERZ and A. L. DREW. *Archives of Neurology and Psychiatry* [Arch. Neurol. Psychiat., Chicago] **63**, 843-874, June, 1950. 33 refs.

The disorder of movement was studied in 6 patients with hepatolenticular degeneration by means of motion-picture analysis. Spontaneous involuntary movements may consist of a regular alternating tremor or may be choreic, athetotic, or dystonic. Alternating tremor may be increased in intensity during the maintenance of postures, and "static intentional tremor" may also occur. The authors consider that cerebellar dysfunction may play some part in the genesis of these disorders of movement.

In cases with a course prolonged over many years little evidence of hepatic dysfunction could be found either clinically or by liver function tests, but in cases with a rapidly progressive course there were obvious symptoms and signs of liver disease. The pathology of the liver was studied in 3 cases; in one there was a chronic cirrhotic process and in the other 2 an acute process with necrotic foci was superimposed on the chronic process, the picture resembling subacute yellow atrophy.

J. W. Aldren Turner

**359. Asymptomatic Unilateral Agenesis of the Cerebellum. [In English]**

C. A. ERSKINE. *Monatsschrift für Psychiatrie und Neurologie* [Mscr. Psychiat. Neurol.] **119**, 321-339, June, 1950. 16 figs., 35 refs.

**360. Subdural Tumours in the Region of the Foramen Magnum. (Tumeurs sousdurales du trou occipital)**

P. MARTIN and E. KLEYNTJENS. *Revue Neurologique* [Rev. neurol.] **82**, 314-334, May, 1950. 7 figs., 22 refs.

Tumours in the region of the foramen magnum are rather uncommon; meningiomata have been found more often in this area than have other tumours such as neurofibromata, fibromata, or myxomata.

The authors record 2 cases of meningioma successfully operated upon; from the relevant literature in addition

to their own experience, they describe the symptoms caused by these tumours.

Pain in the neck, usually the first symptom, may occur several months or even a year or two before neurological signs appear. The first neurological disturbances are usually impairment of sensation, such as numbness, "pins and needles", and a subjective feeling of warmth or cold affecting the occipital region or the neck or the tips of the fingers (later the whole hand) on the side of the lesion. Coughing, sneezing, or even excitement may bring on these dysaesthesiae or make them worse. Subjective disturbances of sensation, at first restricted to the uppermost dermatomes on the affected side, spread later to the opposite side.

Motor impairment starts usually with loss of skilled movements of the homolateral hand and wrist muscles; occasionally the small muscles of the hand atrophy. These motor disturbances appear usually at the same time as the subjective sensory disturbances, or shortly afterwards.

As time goes on, the leg on the same side shows signs of pyramidal disturbance, followed by sensory impairment of the contralateral limbs; later, the contralateral leg shows impairment of motor function, followed finally by similar disturbances in the contralateral arm. Sensory signs, clinically demonstrable, occur comparatively late; these usually take the form of hypoaesthesia or analgesia, or even hyperaesthesia, in the occipital region (C2) or in the area of distribution of C3 and C4 on the side of the lesion.

As soon as the tumour has attained some size, pain and temperature sensation on the opposite side of the body becomes involved (by pressure on the spinothalamic tract). Touch, vibration, and position sense are, as a rule, impaired. Astereognosia or pseudo-astereognosia is described by several observers. Occasionally nystagmus, trigeminal involvement, dysphagia, hoarseness, hypoglossal paresis, ataxia of the homolateral arm, dyspnoea, tachycardia, nausea, and vomiting occur, indicating involvement of the medulla oblongata. Hiccup, paresis of the diaphragm, and atrophy of the sternocleidomastoid are of great localizing value. Atrophy of the small muscles of the hand may lead to an incorrect diagnosis of the level of the lesion.

Radiographs of the cervical spine are not very useful as a rule, but films showing the base of the skull may reveal a deformity of the foramen magnum at the site of the tumour, together with increased or decreased calcification of the adjacent bone.

The use of iodized-oil radiography may be dangerous in these cases; lumbar puncture should be carried out with great caution and may or may not yield significant changes. Study of chronaxia and electromyography might be very valuable, but has apparently never been carried out yet.

The rest of this important paper is dedicated to a discussion of the physiology and pathology of the symptoms, differential diagnosis, and treatment of these lesions.

F. K. Kessel

See also Sections Pathology, Abstracts 126-7; Infectious Diseases, Abstract 393.

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# Psychiatry

## 361. Congenital Malformations in the Teeth and Eyes in Mental Defectives

R. SPITZER. *Journal of Mental Science* [*J. ment. Sci.*] 96, 681-709, July, 1950. 6 figs., 43 refs.

An investigation into the incidence of congenital malformations of the teeth and eyes in association with mental deficiency was carried out on 322 mentally defective patients at two hospitals, cases in which the mental deficiency was obviously the result of birth injury, trauma in early infancy, or congenital syphilis being excluded. With regard to the teeth, only bilateral lesions were accepted, the disorders found being enamel hypoplasia, malformation of shape, and microdontia. The eye changes were mostly lenticular, other conditions found (in one or two cases each) being incomplete persistence of hyaloid artery, persistent pupillary membrane, opaque nerve fibres, inferior crescent, pigment round the disk, gliosis of the disk, and choroideraemia. The changes in the lens consisted of arcuate opacities, dot-like or flake opacities, and suture cataracts. The author concludes that the mental and lenticular disorders are prenatal in origin, that the anomalies of the dentition are aetiologically related to the other congenital defects, and that the factors responsible for the disorders lie in the ectoderm.

G. de M. Rudolf

## 362. The Most Unpleasant Concept Test. A Graphic Projective Technique

M. R. HARROWER. *Journal of Clinical Psychology* [*J. clin. Psychol.*] 6, 213-233, July, 1950. 15 figs., 3 refs.

## 363. Enuresis in Adults and Abnormality of Sleep

R. STRÖM-OLSEN. *Lancet* [*Lancet*] 2, 133-135, July 22, 1950. 7 refs.

In the investigation of 28 cases of enuresis, the author found an associated hypersomnia in 25. The enuresis was fairly severe. The patients scarcely ever manifested anxiety symptoms; in fact, they were usually apathetic. Sleep was very heavy and began immediately on lying down; the patients were difficult to rouse in the mornings. The best therapeutic results were obtained by giving amphetamine or "dexedrine" (D-amphetamine) in 25- to 30-mg. doses at bedtime. Few untoward effects were noted with amphetamine, though it was given for several weeks. The author discusses the nature of the lesion and thinks that sleep might be brought about by a dissociation between the cortex and the hypothalamus. The latter acts as a centre for micturition and is controlled by the cortex. When the cortex is cut off from the hypothalamus, as may occur in deep sleep, incontinence may occur. A lesion between the midbrain and the floor of the third ventricle may cause hypersomnia. It is possible that amphetamine lessens the degree of dissociation between cortex and hypothalamus and allows the former to exert some control over the latter even in sleep.

Paul B. Woolley

## DRUG ADDICTION

## 364. Genetotrophic Diseases; Alcoholism

R. J. WILLIAMS, L. J. BERRY, and E. BEERSTECHEER. *Texas Reports on Biology and Medicine* [*Tex. Rep. Biol. Med.*] 8, 238-256, Summer, 1950. 13 figs., 15 refs.

The authors suggest that alcoholism is a "genetotrophic" disease, that is to say, a diseased state for which genetic factors and nutritional deficiency are jointly responsible, and that if a partial genetic block of a metabolic process creates an abnormally large requirement for a substance (such as a vitamin), a relative deficiency of that substance in the food may secondarily create an abnormal appetite for alcohol. As evidence supporting this hypothesis the authors report experiments carried out with rats and mice which showed that when the animals could choose between water and 10% alcohol to drink, the alcohol intake depended on several factors, including the nature of the diet and the strain of animal. [Since, even within highly inbred strains, individuals may differ greatly from each other, the genetic differences between strains are not very convincingly demonstrated, although they may well be real.] On a restricted diet, the rats consumed more alcohol than on the same diet supplemented by the vitamins of the B group. The authors think that it should be possible to abolish the appetite for alcohol altogether in laboratory animals by liberal addition of those nutritional factors in which ordinary stock diets are supposed to be relatively deficient for animals of certain genotypes.

H. Grüneberg

## 365. Biochemical Methods in the Treatment of Alcoholism, with Special Reference to Antabuse

E. JACOBSEN. *Proceedings of the Royal Society of Medicine* [*Proc. R. Soc. Med.*] 43, 519-526, July, 1950. 10 figs., 20 refs.

The author discusses the treatment of alcoholism, which must be directed towards the adjustment of internal factors, the withdrawal of alcohol, and the adjustment of external factors. He describes the technique employed in Denmark by Martensen-Larsen, who was the first to use "antabus" (tetraethylthiuram disulphide) clinically. In addition to the administration of antabus, the nature of alcohol addiction is explained to the patient, and individual psychotherapeutic sessions are given; group therapy is used, an association on the lines of Alcoholics Anonymous has been formed, and a guardian for each patient is appointed.

Of the first series of 169 patients treated with antabus, the majority were males aged about 40 years, married and with children, were employees in business, and had a fixed home. The most frequent aetiological factors found were alcoholism in the family, heavy drinking in the milieu, slight psychoneurotic tendency, and a need to compensate for disabilities. There was no abuse of

other drugs, and for most patients the critical dose of alcohol was low. Periodic drinkers were the most common, from £100 to £200 per annum was the usual expenditure on alcohol, and those who drank mainly away from home outnumbered the home drinkers. About equal numbers had been alcoholic for 6 to 10, 11 to 20, and over 20 years; the majority had come into conflict with the law owing to alcoholism, and 93 had suffered a decrease of up to one-quarter of their social efficiency. The average critical dose (which is the quantity required to drive the patient to further drinking) was the equivalent of 10 to 20 ml. of absolute alcohol.

Patients with small decrease in social efficiency, younger patients, and those with little or no sign of psychoneurosis gave the best results. At the end of 9 months 82% of the patients who had taken antabus regularly for 6 months had recovered socially, whereas of those who had taken antabus only occasionally only 35% had recovered. Amongst patients who continued the treatment for 2 months, 67% reported social recovery, the proportion being higher when the relatives were co-operative. Psychotherapy consists in encouragement to continue taking antabus for a sufficient time, the finding of new interests to replace the gap left by the stopping of drinking, and the treatment of the mental troubles which had led to drinking. Within 3 months of the beginning of treatment an improvement occurs which may cause the patient to stop taking antabus unless care is taken. Antabus makes the treatment of alcoholism more encouraging, but not any easier, the results being largely determined by the quality of the psychological and social treatment given to each patient. *G. de M. Rudolf*

**366. Biological Treatment of Chronic Alcoholism with Apomorphine. Study of 150 Cases.** (Le traitement biologique de l'alcoolisme chronique par l'apomorphine. Étude de 150 cas)

G. DE MORSIER and H. FELDMANN. *Schweizerische Medizinische Wochenschrift* [Schweiz. med. Wschr.] **80**, 465-467, May 6, 1950. 3 refs.

According to the individual case, the treatment of alcoholism with apomorphine as practised by the authors lasts from 2 to 10 days; it suppresses the euphorizing effect of alcohol and the desire to drink, and induces an active distaste for alcohol through the creation of a conditioned reflex. The production of nausea and vomiting is not essential for good results to be obtained. After 3 or 4 days the influence of apomorphine on nervous symptoms becomes apparent, the patient thus becoming more approachable for psychotherapy. It is emphasized that apomorphine has a direct action on the nervous centres and does not work through a reflex action from the stomach. It acts not only on the vomiting centres, but also on those diencephalic centres which are related to emotivity, affective reactions, nutritive instincts, and impulsions. Apomorphine does not provoke addiction, but the organism becomes sensitized to its effect. The authors analyse the results in the first 150 of their 270 cases consisting of 126 men and 24 women, not specially selected, and observed for at least 8 months. Most relapses occur within the first 6 months. After 8 months

the patient may be regarded as successfully detoxicated. The results were somewhat better among women (44% of the men and 54% of the women are considered by the authors to have been cured). Matrimonial difficulties seem to play an important part in relapse, whereas the mental state does not play such a role, with the exception of constitutional or irreversible psychiatric or psychological troubles.

[The authors claim to have cured 46% of their 150 patients, but do not define what they regard as a "cure"; it is the general opinion that several years should have elapsed before a "cure" can be claimed; most of the patients referred to in this paper, however, have been observed for a much shorter period and therefore the percentage of "cured" patients may still be corrected as time progresses. However, there is no doubt that apomorphine treatment can be a great help in many instances, economizing in time and expense.]

*P. O. Wolff (Excerpta Medica)*

**367. Death during Anti-alcoholic Treatment with Tetraethylthiuram disulphide.** (Un cas de mort pendant le traitement par une médication antialcoolique)

D. FURTADO, V. CHICHORRO, and O. DE CARVALHO. *Presse Médicale* [Pr. méd.] **58**, 795-796, July 8, 1950. 2 figs., 6 refs.

A man of 49 was admitted to hospital in Lisbon with the diagnosis of chronic alcoholism, with defective memory and some loss of social sense and of intellect. Physical examination showed no abnormality except a slightly enlarged, but painless, liver. Neurologically, there was marked alcoholic tremor and much difficulty in articulation. Mentally, there was dulling of the intellect, with impairment of orientation in space and time. Memory was accurate for events long past, but was greatly impaired for recent happenings. Laboratory tests showed hepatic and renal functions to be normal, and nothing abnormal was found in the blood, the urine, or the cerebrospinal fluid. The patient was given a very rich diet, with vitamin supplements parenterally, and in a fortnight had improved greatly, becoming more lucid and alert and remembering things more easily. He was then given "antabus" (tetraethylthiuram disulphide) in doses of 0.25 g. rising to 0.75 g. a day for 11 days. On the last of these days he was allowed half a litre of wine, and the usual circulatory reactions occurred. It was noticed at the end of the test and subsequently that he seemed somewhat sleepy, and during the next few days the drowsiness increased and the drug was stopped. He made no complaint of headache, and the fundi were normal. On the seventh day after the test he became comatose, with profound circulatory collapse, and died.

At necropsy, apart from bronchopneumonia at the left base and generalized pulmonary oedema, the viscera appeared normal. There was some thickening of the meninges and flattening of the cerebral convolutions and on sectioning the brain after hardening, a mass of blood about 3 cm. in depth was found in the posterior part of the right hemisphere. There was no nervous tissue in the mass, which was of the nature of a haematoma. Another, smaller, haematoma was found about the middle of the left callosal gyrus. No explanation of the causa-



tion of these haemorrhages is offered, but the authors refer to a somewhat similar case recently reported, also from Portugal. They express the opinion that this method of treatment should be regarded as still in the experimental stage and its use confined to certain specialized centres.

Reginald St. A. Heathcote

### 368. Chronic Barbiturate Intoxication: an Experimental Study

G. ISBELL, S. ALTSCHUL, C. H. KORNETSKY, A. J. EISENMAN, H. G. FLANARY, and H. F. FRASER. *Archives of Neurology and Psychiatry* [Arch. Neurol. Psychiat., Chicago] 64, 1-28, July, 1950. 1 fig., bibliography.

The aim of this investigation was to study the phenomena of chronic barbiturate intoxication, and to ascertain whether withdrawal symptoms are due to the abstinence from barbiturates alone, or whether other factors, such as withdrawal of other drugs to which addiction had been formed, malnutrition, or special personality traits, are responsible. The subjects of the investigation were 5 former morphine addicts who were serving prison sentences and who volunteered to undergo the experiment. They were given increasing doses of "seconal", pentobarbitone ("nembutal"), or amylobarbitone ("amytal") until a continuous mild or severe intoxication was established, which was maintained for periods ranging from 92 to 144 days.

The signs of chronic barbiturism showed some variation from person to person and from day to day, the latter variation being partially related to changes in food intake. There were no significant abnormalities in the blood or urine. The withdrawal of barbiturates was abrupt and complete and was followed by withdrawal symptoms for 12 to 13 days. During the first 12 to 16 hours after the last dose of barbiturate the subjects' condition improved. Then anxiety, tremor, weakness, abdominal distress, and vomiting developed, convulsions occurred in 4 cases, and 4 subjects developed delirious symptoms. All the subjects recovered completely within 60 to 90 days. After recovery, 4 of the subjects were again given barbiturates in the maximum dosage attained during the experiment; administration caused severe neurological and psychological symptoms and had to be discontinued. This is interpreted as indicating that some tolerance had developed during the phase of chronic intoxication, but had since been lost.

F. K. Taylor

### 369. Addiction to Barbiturates and the Barbiturate Abstinence Syndrome

H. ISBELL. *Annals of Internal Medicine* [Ann. intern. Med.] 33, 108-121, July, 1950. 20 refs.

Chronic intoxication with barbiturates occurs as a true addiction in neurotic and psychopathic individuals, who are often also addicted to other drugs. The patients show intellectual impairment, emotional lability, depression, and disregard of personal appearance and cleanliness. They usually remain, however, oriented in time, place, and person, and seldom have hallucinations or delusions. The neurological signs include ataxia, dysarthria, nystagmus, tremor, transient ankle clonus,

and positive Babinski sign. The electroencephalogram reveals an increase in  $\beta$  waves (15 to 30 per second) which may be of diagnostic value in doubtful cases.

Abstinence symptoms develop 12 to 16 hours after withdrawal. The patients become weak and apprehensive, have coarse tremors, cannot sleep, have abdominal cramps, and may vomit frequently. Epileptic convulsions and minor episodes may occur. Between the third and seventh days a delirious psychosis may develop resembling an alcoholic delirium tremens. The kind and intensity of these abstinence symptoms vary considerably, however, from patient to patient.

Therapeutic withdrawal of barbiturates must be gradual, extending over 2 to 4 weeks, and carefully supervised. If paroxysmal slow activity appears in the electroencephalogram, the withdrawal of the drug should be temporarily stopped.

Recurrence of the addiction is very likely, and prolonged psychotherapy is indicated.

F. K. Taylor

## TREATMENT

### 370. Electronarcosis: a Safe Technique for Routine Administration under Anaesthesia and Eulissen (Decamethonium Iodide or C.10)

C. R. HARRIS. *Journal of Mental Science* [J. ment. Sci.] 96, 788-792, July, 1950. 5 refs.

The dangers associated with electronarcosis (which the author believes to have been unduly emphasized) can be greatly reduced by the administration of thiopentone and decamethonium iodide. Of 70 patients who received a total number of 600 treatments with this technique none suffered from any serious complication. The technique and equipment used are described in detail and it is recommended that a skilled anaesthetist should be included in the treatment team. Thiopentone (0.4 to 0.6 g.) and decamethonium iodide (1.5 to 5 mg.) are given intravenously, mixed together, 1½ minutes before the current is switched on, producing muscular relaxation and continuous anaesthesia. D-Tubocurarine was tried at first, but it was found that decamethonium iodide has a quicker action and does not involve the respiratory muscles to the same extent. The paper is not concerned with the results of treatment, but it is mentioned briefly that striking results have been achieved by this method where other methods have failed.

J. T. Leyberg

### 371. Changes Continuing after the Termination of Treatment of Mental Defectives with Aneurin

G. DE M. RUDOLF. *Journal of Mental Science* [J. ment. Sci.] 96, 796-798, July, 1950. 5 refs.

In previous reports (*J. ment. Sci.*, 1949, 95, 910; 1950, 96, 265 and 272) the author has drawn attention to the improvement in the behaviour, intelligence quotient, and social age of mental defectives treated with aneurin for a period of 6 or 12 months. In this short paper it is claimed that in some cases this improvement can be observed for up to 14 months after the termination of treatment.

J. T. Leyberg

### 372. Clinical Observations on Tolserol in Handling Anxiety Tension States

H. H. DIXON, H. A. DICKEL, R. A. COEN, and G. B. HAUGEN. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 220, 23-29, July, 1950. 9 refs.

The authors report their observations in 124 cases of anxiety treated with "tolserol" (mephensin or "myanesin") in doses of from 0.25 to 6 g. The patients, aged from 20 to 60 years, were actively engaged at the time of treatment in housekeeping, managing businesses, or practising a profession. Within 35 minutes of administration of the drug the patients felt they could "let go". Sensations of warmth, of numbness, and of pins and needles were reported. In some cases there was blurred vision, drowsiness, muscular incoordination or euphoria. A few patients reported gastro-intestinal distress. In all except a very few there was a dramatic termination to the feeling of anxiety. The relief lasted for 2 to 3 hours with the doses given, the average dose being from 0.75 to 1.5 g. daily for 10 days. Tolserol was used so that patients would experience the state of complete relaxation. It had no effect on individuals already relaxed. There was no difference in the action of the drug whether it was given in tablets or as an elixir.

[Kositchek and Barnet (*J. Amer. med. Ass.*, 1950, 143, 22) reported a case of temporary anaemia, abdominal pain, and nausea following the administration of 50 g. of tolserol in 13 days.] G. de M. Rudolf

### 373. Observations on the Effect of Myanesin (3-ortho-Toloxyl-1:2-propanediol or Tolserol) on Epileptic Thresholds and Some Psychiatric Conditions

R. K. FREUDENBERG. *Journal of Mental Science* [J. ment. Sci.] 96, 751-757, July, 1950. 18 refs.

The effect of mephensin ("myanesin") on the convulsive threshold was studied in patients undergoing electric convulsion therapy (E.C.T.) and leptazol shock treatment. The previous administration of mephensin in doses of 1 g. given  $\frac{1}{2}$  hour before treatment, 5 g. having been given the day before, raised the convulsive threshold for electrical stimulation to a statistically significant degree, while with higher doses of mephensin E.C.T. did not cause major attacks in some cases. The increase in threshold was less evident when leptazol was used to induce convulsions, this drug appearing to have an antagonistic action to mephensin. The beneficial effect of depressant action of mephensin on the cerebral cortex was also demonstrated in cases of anxiety state, and in reducing tremor and hallucinations of alcoholic delirium tremens. Mephensin may thus prove to be a useful drug in psychiatric treatment; further research is indicated.

J. T. Leyberg

### 374. Does Glutamic Acid Administration Influence Mental Function?

H. G. LOEB and R. D. TUDDENHAM. *Pediatrics* [Pediatrics] 6, 72-77, July, 1950. 11 refs.

The authors describe an investigation into the effect on the mental function of retarded persons of the administration of glutamic acid, favourable results having been reported several times during the past

5 years, especially by Zimmerman *et al.* (*Arch. Neurol. Psychiat.*, Chicago, 1946, 56, 489). They selected 33 adolescent patients, mostly between the ages of 10 and 17, with unequivocal feeble-mindedness and without epilepsy or other neurologic involvement, and divided them into two groups which were approximately comparable in respect of the sex distribution, average age and Stanford-Binet I.Q., and types of feeble-mindedness represented. As preliminary psychometric appraisals showed no significant difference between cases of primary and secondary feeble-mindedness, both types were included in the investigation. The experimental group consisted of 18 patients (12 males and 6 females), 5 with primary and 13 with secondary feeble-mindedness, whose average age was 15 years, 2 months. The control group contained 15 patients (10 males, 5 females), 4 with primary and 11 with secondary feeble-mindedness, whose average age was 13 years, 9 months. After a battery of psychological tests of mental ability had been applied to all the patients, the members of the experimental group were given the monosodium salt of glutamic acid (in 40% solution flavoured with peppermint) in daily doses of 12 g. on the first day, 18 g. for the next 6 days, and 24 g. for the following 16 weeks, after which the tests were repeated. The controls were given a placebo of peppermint-flavoured distilled water in similar doses under the same conditions. During the whole of the investigation both experimental and control subjects remained in the same institution and received the same care and diet, the food being prepared in a central kitchen.

It was found that none of the psychological tests demonstrated any statistically significant difference in intelligence or performance ability between the two groups as a result of treatment. Nor were any significant subjective impressions reported. The authors point out that although they gave the neutral sodium salt of glutamic acid instead of the free acid, the amount of sodium given could not seriously alter the physiological situation, so that they consider their experiment to be comparable with those of Zimmermann and others. They suggest that differences in the degree of experimental control, in the design of the investigation, and in the nature of the statistical analysis of results may account for the difference in findings. Myra Mackenzie

### 375. The Effect of Glutamic Acid Feeding on Cognitive Abilities of Institutionalized Mental Defectives

T. L. MCCULLOCH. *American Journal of Mental Deficiency* [Amer. J. ment. Defic.] 55, 117-122, July, 1950. 12 refs.

### 376. Cerebral Dysrhythmia Induced by Photic and Chemical Stimulation as a Method of Treatment in Psychiatry

P. O'FLANAGAN, P. W. SMITH, and R. B. TAYLOR. *Journal of Mental Science* [J. ment. Sci.] 96, 745-750, July, 1950. 2 figs., 9 refs.

At the Pastures Hospital, Mickleover, Derby, the authors have treated 15 cases of depression and 5 of schizophrenia by the induction of cerebral dysrhythmia by photic and chemical stimulation. The technique consists in giving an intravenous injection of 1 ml. of

5% leptazol in aqueous solution, followed 5 to 15 seconds later by intermittent photic stimulation from a stroboscope, usually at a frequency of 15 flashes per second. Initial periods of stimulation lasting 1 to 5 seconds are given at approximately 5-second intervals, the periods being progressively lengthened up to 1 minute as the effect of the leptazol wears off. By adjustment of the duration of exposure to the flicker, the patient can be kept at the stage of myoclonus without the development of a full convulsion. If the patient is not improving, photic stimulation is continued uninterruptedly until a convulsion occurs. Treatment is given 2 or 3 times each week. Electroencephalographic control is not essential, although of interest. The results in this limited series bear favourable comparison with those of electric convulsion therapy.

G. de M. Rudolf

**377. Intelligence Tests and Rorschach Tests on Patients after Prefrontal Lobotomy.** (A praefrontalis lobotomia eredményeiről. II. Intelligencia-és Rorschach-vizsgálatok praefrontalis lobotomián átesett betegeken) J. IRÉN. *Orvosi Hetilap* [Orv. Hetil.] **91**, 938-942, July 23, 1950. 3 figs.

A series of ten intelligence tests designed to estimate powers of logical reasoning, practical ability, concentration, and memory, and a Rorschach test were performed on each of 25 patients before and after, and on 6 after, prefrontal leucotomy. Average percentage markings for the whole group of intelligence tests were ascertained; in no case before operation did the mark exceed 40% in all mentally ill patients, 30% in patients suffering from depression, or 15% in schizophrenic patients. It was recognized that potential intelligence was not tested. After operation 7 patients showed no increase in ability to carry out the tests, and all these patients had to be retained in the institution. A further 7 could score only 15% and of these, 4 remained in an institution. Eight achieved a marking of up to 39% and these could be discharged; 9 who scored over 40% were all symptom-free. The Rorschach tests showed significant changes towards normality after leucotomy. It is concluded that the operation does not decrease intellectual performance, but rather makes available potentialities of intelligence previously eclipsed by pathological states of mind. Dushanka Wolstenholme

**378. Development of Psychosurgery.** (K vývoji psychochirurgie) J. SEMOTÁN. *Rozhledy v Chirurgii* [Rozhl. Chir.] **29**, 187-193, 1950.

The evolution of psychosurgery is traced, with special emphasis on the pioneer work done on the subject by Knobloch, in Prague, 266 patients operated on at his neuropsychiatric clinic over 4 years forming the basis for the observations in this article. Prefrontal lobotomy gave good results in cases of depression (except the involuntal forms), catatonic and paranoid schizophrenia, obsessional states, and some cases of intractable pain. The affective psychoses, where advanced personality changes have not taken place, are most improved and a limited operation is usually adequate. The lower-

grade psychoses with more advanced personality changes were found to require more extensive operations, either of the standard Freeman-Watts, or the radical Freeman-Watts type as modified by Knobloch. The age, sex, and length of history did not affect the prognosis, the choice of operation being largely determined by the state of the patient's personality. Unilateral operations were unsatisfactory in all cases. Post-operatively, apart from psychiatric changes usually in the desired direction, autonomic disturbances were noted, such as enuresis, vasomotor changes, and trophic changes. An adequate follow-up is essential, as improvement may continue for 1 to 12 months after the operation. Of the patients 65% were definitely improved. Others derived more limited benefit, but on the whole results were gratifying. Operative mortality was 3%. Apart from the purely psychiatric and surgical factors, the patient's home environment must be studied. Finally, an occupation suited to his mental capabilities must be found. Thus a rehabilitation centre is an important link in the patient's progress from the institution to the unsheltered life of the outside world.

J. Kodlíček

**379. A Follow-up Investigation of 330 Cases Treated by Prefrontal Leucotomy**

E. STENGEL. *Journal of Mental Science* [J. ment. Sci.] **96**, 633-662, July, 1950. 9 refs.

The author reports the results of a clinical follow-up investigation carried out on 330 out of a total of 345 patients who underwent prefrontal leucotomy at Graylingwell Hospital, Chichester, between October, 1942, and December, 1947. The technique used was that of Freeman and Watts, all the operations being performed by the same surgeon. All patients after operation received intensive occupational therapy, took part in planned social activities, and were given supportive psychotherapy wherever possible [and consequently the results may not have been due entirely to the operative procedure]. The follow-up examination in each case consisted of one or two psychiatric interviews, at least one year being allowed to elapse after the operation before the patient was examined. The relatives were interviewed by a psychiatric social worker.

Of 209 patients with schizophrenia or paranoia, 74 had been discharged, 115 were still in hospital and 20 were dead. Of 95 patients with affective reaction types of psychosis, 74 had been discharged, 8 were still in hospital, and 13 were dead. Of 28 cases of schizophrenia in which operation resulted in full remission, 7 were of the catatonic and 15 of the paranoid type. In 13 out of 16 cases of recurrent depression, 18 out of 24 cases of manic-depressive reaction, and 25 out of 33 cases of involuntal depression full remission was obtained. The usual personality change associated with a frontal-lobe lesion took place in 19 of the 22 cases of schizophrenia and in all except 5 of the 56 cases of the affective reaction types in which there was complete remission. Fits occurred in 11% of all cases treated, at intervals up to 5 years after operation. Of the 14 patients who had died after operation and the 20 who had died after discharge, 11 died from causes associated with the surgical treatment.

G. de M. Rudolf



# Infectious Diseases

## VIRUS INFECTIONS

### 380. Attempts to Isolate Poliomyelitis Virus from the Paralyzed Muscle of Patients during the Acute Stage of the Disease

C. W. JUNGBLUT and M. A. STEVENS. *American Journal of Clinical Pathology* [Amer. J. clin. Path.] **20**, 701-706, Aug., 1950. 4 figs., 17 refs.

Biopsy material was obtained from the paralyzed quadriceps muscle of a small boy during the acute stage of poliomyelitis, and the ground-up muscle was injected intracerebrally into cynomolgus monkeys. Three passages were carried out by intracerebral inoculation of cynomolgus monkeys. The virus thus isolated produced myocarditis and, when injected intramuscularly into a cynomolgus monkey, myositis, as well as typical lesions in the anterior horn cells.

G. M. Findlay

### 381. Electrophrenic Respiration in Acute Bulbar Poliomyelitis: its Use in Management of Respiratory Irregularities

S. J. SARNOFF, J. V. MALONEY, L. C. SARNOFF, B. G. FERRIS, and J. L. WHITTENBERGER. *Journal of the American Medical Association* [J. Amer. med. Ass.] **143**, 1383-1390, Aug. 19, 1950. 7 figs., 29 refs.

For some time it has been apparent that in poliomyelitis less relief is to be expected from artificial respiration in the "iron lung" in those cases in which the bulbar centres are seriously affected than in those where damage is located solely in the spine. The present authors discuss the reasons for this failure, and endeavour to assess the value in treatment of direct stimulation of the phrenic nerve by means of an electrode placed over its motor point, or even surgically embedded in the neck.

From experience based on 9 cases so treated, they point out that irregularities in respiratory rhythm [well-called "respiratory fibrillation"] can be suppressed by electrophrenic stimulation, and at the same time effective and regular ventilation can be obtained. Whereas more forcible pressure gradients may perhaps increase the usefulness of a tank respirator in certain cases of bulbar poliomyelitis, it must be borne in mind that such increased pressure may actually worsen the state of a patient whose circulation is in poor condition. Electrophrenic stimulation, on the other hand, while introducing no new hazard, may raise blood pressure and increase cardiac output.

In spite of their encouraging results the authors do not yet feel able to claim that the usefulness of electrophrenic respiration in bulbar paralysis has been completely established. The apparatus is, it seems, not well adapted for inexperienced hands; moreover [as indeed seems obvious] one phrenic nerve at least must be partially free from disease if any result is to be expected. One good effect which the authors claim to have observed is a marked

diminution in restlessness and the spasms of hypertension which are so often noted in bulbar paralysis.

[Though bulbar paralysis is the most immediately fatal form of the disease, it is the one in which the greatest degree of recovery may be obtained if only the patient can be tided over the acute phase. It would seem, therefore, that the method of treatment described in this excellent paper merits the closest study by all concerned.]

Joseph Ellison

### 382. Patterns of Plasma Protein Changes in Acute Poliomyelitis Patients: Treatment with Blood Plasma

A. G. BOWER, R. M. EATON, J. S. CHUDNOFF, J. E. AFFELDT, and A. L. CHANEY. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] **220**, 46-54, July, 1950. 7 figs., 12 refs.

The serum protein patterns were studied in 75 confirmed cases of acute poliomyelitis occurring during the Los Angeles epidemic of 1948. Of these cases, 47 were treated as a control group and were divided, on the basis of an arbitrary classification devised by the authors, into 9 severe, 13 moderate, and 25 mild cases of poliomyelitis, depending on the degree of muscular involvement. The remaining 28 patients, similarly classified as 15 severe, 9 moderate, and 4 mild cases, received daily infusions of pooled, irradiated, human blood plasma at a dosage of 5 ml. per lb. (11.1 ml. per kg.) body weight.

Serum protein level was frequently estimated in all cases in the series and results showed that, in the control series, the serum albumin level fell progressively in a manner roughly parallel to the severity of the illness, the fall beginning between the first and third days and reaching a maximum between the seventh and tenth days of the illness. This fall in serum albumin level was retarded in the treated series by the administration of plasma; indeed it was reversed in the mild cases with the dosage employed. However, this dosage, though helpful, was inadequate in the severe cases. The increase in serum albumin concentration caused by the plasma intake was a temporary effect, and continuous administration was needed for sustained results; the period of such administration was not determined.

In both the control and treated series the serum globulin values began to rise early in the illness, especially in the moderate and severe cases, resulting at times in a reversal of the albumin-globulin ratio. The authors, while recognizing the danger of formulating opinions on insufficient data, believe that giving blood plasma in clinically moderate and severe cases of acute poliomyelitis is definitely valuable, and tabulate their results according to the change in muscular involvement which occurred between the 3rd and 14th days of the illness. In the plasma-treated group results were superior on the basis of the method of evaluation used by the authors, particularly in the group of severe cases [but additional evidence would seem to be necessary].

R. P. Hullin

**383. A Case of Rabies with a Prolonged Incubation Period and an Unusual Variation Phenomenon of the Virus Isolated therefrom. [In English]**

D. USHIBA, K. ABE, J. TANAKA, and K. HORIE. *Japanese Medical Journal [Jap. med. J.]* 2, 177-184, Aug., 1949. 1 fig., 9 refs.

An incubation period of a year for rabies has previously been recorded. A girl, aged 6 years, while living in Tokyo, was bitten on the face by a mad dog on July 15, 1945. She was not treated with rabies vaccine and the wound healed within 14 days. On Jan. 12, 1948, 911 days after the bite, she developed typical symptoms of rabies and died on the third day of her illness. A rabies virus was recovered from her brain and passaged in mice and rabbits, where it rapidly became fixed. During the interval between the bite and the development of rabies, the girl had no association of any sort with animals.

G. M. Findlay

**384. Influenza A Prime: a Clinical Study of an Epidemic Caused by a New Strain of Virus**

E. D. KILBOURNE and J. P. LOGE. *Annals of Internal Medicine [Ann. intern. Med.]* 33, 371-379, Aug., 1950. 2 figs., 16 refs.

Influenza viruses have been intensively studied in the laboratory during the last 10 years, but, with surprisingly few reports of clinical investigations, the pathological picture in man remains ill-defined. The authors describe in detail clinical and laboratory observations on 76 patients with influenza-A prime infection, admitted to hospital during the peak of an epidemic at Fort Monmouth, New Jersey, in February, 1947. Details are also given of 367 patients admitted during the same period with non-viral upper respiratory infections. Few significant differences in signs and symptoms were observed on comparing cases of established influenza with cases of upper respiratory infection accompanied by the presence of  $\beta$ -haemolytic streptococci; conjunctival burning and epistaxis, however, were far more common in the influenzal cases. There were no serious complications, the clinical course of the disease being acute but usually of only 2 to 3 days' duration. Signs of lower respiratory tract infection were detected in only 3 cases. In general the findings agree with the earlier descriptions of influenza as an acute, benign, febrile disease of abrupt onset, accompanied by prostration, headache, and dry cough. Constitutional reactions are often disproportionate to the physical signs, but secondary pneumonia is rare.

Towards the end of the influenza epidemic the authors observed a considerable increase in the proportion of patients admitted carrying haemolytic streptococci, and in the following month an epidemic of streptococcal pharyngitis ensued. This is an interesting observation, since it has been shown experimentally that ferrets infected with influenza-A virus may become susceptible to strains of streptococci, which normally are incapable of invading the ferret's nasal mucosa. The authors suggest that a similar virus-host relationship may exist between influenza-A prime virus and  $\beta$ -haemolytic streptococci in man.

J. F. McCrea

M—H

**385. Clinical Trials of Antihistaminic Drugs in the Prevention and Treatment of the Common Cold**

SPECIAL COMMITTEE OF THE MEDICAL RESEARCH COUNCIL. *British Medical Journal [Brit. med. J.]* 2, 425-429, Aug. 19, 1950. 17 refs.

These clinical trials by the Medical Research Council demonstrate conclusively that when steps were taken to eliminate every possible source of bias, the antihistaminic drugs tested had no value in either the prevention or the treatment of the common cold. The investigation was based on standards laid down in the similar trial of patulin (*Lancet*, 1944, 2, 373).

The first experiment, in prophylaxis, was carried out at Salisbury, where paired volunteers were given either "histantin", 50 mg. twice daily starting 48 hours before inoculation with virus and continuing for 72 hours afterwards, or "phenegan", 20 mg. twice daily 60 hours before inoculation and continuing for the same period; both these drugs have strong antihistaminic action. An equal number of controls were given identical tablets containing  $\frac{1}{4}$  gr. (16 mg.) of phenobarbitone. Although the numbers were small, the experiment was carefully controlled, and there is no reason to doubt the validity of the negative results obtained.

Therapeutic trials were conducted between March and May, 1950, at 19 centres in Britain with a total population of 50,000. The method was carefully standardized: all volunteers were over the age of 15, complications and allergic manifestations were excluded so far as possible, and a special effort was made to keep secret the identity of the tablets a particular patient received. This was done by a novel method of central coding, whereby the identity was known only to those in the Council's Statistical Research Unit. Thonzylamine was given in doses of 50 mg. three times a day for 3 days because of its low toxicity and reported efficacy. Records were kept of progress at 24 hours, 48 hours, and one week: the evidence obtained was, of necessity, largely subjective. Quinine-lactose tablets, identical in appearance, were given to controls.

Adequate records were obtained from 1,156 persons—579 treated and 577 controls—and these were analysed according to percentage cured and improved, different centres, a previous allergic history, time between onset and start of treatment, and reactions. No significant effect of thonzylamine could be demonstrated, and "indeed the similarity in response of the two groups seems more remarkable than any dissimilarity". Side-effects were similar in both treated subjects and controls and were probably attributable to the cold itself.

A. Paton

**386. Trial of Antistin in the Common Cold**

G. LORRIMAN and W. J. MARTIN. *British Medical Journal [Brit. med. J.]* 2, 430-431, Aug. 19, 1950. 4 refs.

"Antistin" as a therapeutic agent against the common cold was investigated under conditions similar to those which governed the trials of the Special Committee of the Medical Research Council (see Abstract 385). During the period November, 1949, to April, 1950, volunteers reporting within 24 hours of the

onset of a cold were given two tablets of "antistin", and a further tablet was taken every 4 hours except during the night. Controls received tablets which were of identical appearance and practically identical taste, but which contained small doses of quinine. Records were compiled for 1,744 persons, but only 745 of these records were complete—379 treated patients and 366 controls. Analysis failed to show that "antistin" had any significant effect on the course of the common cold. Side-effects were minimal.

A. Paton

**387 (a). Forms of Inclusion Urethritis and Their Pathological Relationships: the Syndrome of Reiter, Fiessinger and Leroy: Fanconi's Syndrome and Atypical Pneumonias.** (Les urétrites à inclusions et leurs parents morbides: le syndrome de Reiter, Fiessinger et Leroy; le syndrome de Fanconi et les pneumonies atypiques)

H. THIERS. *Lyon Médical* [*Lyon méd.*] **183**, 33-39, July 16, 1950.

**387 (b). A Case of Inclusion Urethritis, Clinically Latent during the Evolution of Fanconi's Syndrome.** (Découverte d'une urérite à inclusions cliniquement latente au cours de l'évolution du syndrome de Fanconi)

H. THIERS and —, PINET. *Lyon Médical* [*Lyon méd.*] **183**, 49-50, July 23, 1950.

**387 (c). Inclusion Urethritis due to Faecal Contamination.** (Urérite à inclusions par contamination d'origine fécale)

H. THIERS. *Lyon Médical* [*Lyon méd.*] **183**, 50, July 23, 1950.

**387 (d). Reiter's Syndrome with Inclusion Urethritis, Transient Pulmonary Infiltration and Keratoderma.** (Syndrome de Reiter avec urérite à inclusions, infiltrat pulmonaire labile et kératodermie)

H. THIERS and —, PINET. *Lyon Médical* [*Lyon méd.*] **183**, 51-55, July 23, 1950. 2 figs.

These four communications from Lyon all deal with various forms of inclusion urethritis. The first paper gives a general summary of the present position, with special reference to the recent work of Harkness. It is considered that two types of inclusion may occur, one due to pleuropneumonia-like organisms, the other to a virus having a close similarity to viruses of the lymphogranuloma-psittacosis group.

The second paper describes the case of a woman, aged 53 years, who 2 years previously had suffered from asthma and attacks of polyarthritis which had disappeared after a short time. Her present illness began with a rhinopharyngitis, a return of the asthma, and bouts of coughing, almost like a mild whooping-cough. She had one attack of diarrhoea and also a vaginal discharge without cystitis. Gonococci were absent from the vaginal discharge but scrapings from the urethral mucosa contained cells with cytoplasmic inclusions.

In the third paper the case of a market-gardener with non-specific urethritis is discussed. He was accustomed to collect human faeces from the privies of his neighbour and to use these faeces, undiluted, for the intensive culture of vegetables. He developed fever (temperature 40° C.), sore throat, and cough, and when these had subsided, a non-specific urethritis. [The only evidence

in favour of the faecal source of his infection is that pleuropneumonia-like organisms, non-pathogenic, have been found in soil and in manure.]

In the fourth paper a typical example of Reiter's syndrome is described in a man aged 42 years. Urethral discharge without gonococci, swollen joints, balanitis, and keratoderma were present but there was no eye involvement. There was no history of any diarrhoea or dysentery and no agglutinins for dysentery bacilli were present: the serological reactions for syphilis were negative and cold agglutinins were absent. The temperature was 37.5° to 38.0° C. and at the same time a cough developed with fine crepitations and rales scattered over the left lung. Radiography revealed first, thickening in the left hilar region and then, as the other clinical symptoms disappeared, a diffuse peribronchial infiltration of the left lower lobes unaccompanied by any clinical symptoms. These pulmonary signs cleared up spontaneously. Inclusions were found in the cytoplasm of mononuclear cells in urethral scrapings. Aureomycin failed to improve the symptoms, except the balanitis, in this patient but the symptoms began to clear up when dihydrostreptomycin was combined with *p*-aminosalicylic acid (PAS). Dihydrostreptomycin was given intramuscularly in doses of 1 g. daily, PAS daily by mouth in a dose of 10 g. of the sodium salt. A slight urethral discharge still persisted but this is said to have disappeared on administration of an antigen formed from the urethral pus.

G. M. Findlay

## BACTERIAL INFECTIONS

**388. Thiosemicarbazone in the Treatment of Leprosy**

G. A. RYRIE. *Lancet* [*Lancet*] **2**, 286-287, Aug. 19, 1950. 1 ref.

The results of treatment of 10 cases of leprosy with "thiacetazone" (*p*-acetylaminobenzaldehyde thiosemicarbazone) are described. There were 8 males and 2 females, all adults. Eight of the cases were said to be of a "virulent lepromatous type" and 2 of the tuberculoid type. Some had had previous sulphone therapy. Treatment was begun at a level of 50 mg. of the drug daily, rising gradually to 150 mg. given orally in 25-mg. tablets. Varying degrees of improvement in individual cases are reported. In one lepromatous case the nodules flattened out and bacilli disappeared in 4 weeks. In other cases the lesions receded and the bacillary content decreased. It was not easy to decide how much of the improvement was due to the thiosemicarbazone. Fluctuations in the course of the disease and possible effects of previous sulphone therapy had to be taken into account. The only symptom of toxicity was a complaint of gastric uneasiness by one patient who was receiving 150 mg. daily. When the dose was cut by half this symptom disappeared.

The author comments particularly on the absence of mental depression, which he has found such a drawback to sulphone therapy. He admits that the period of observation of this series of cases was utterly inadequate, but in view of the rapid improvement and the known antibiotic effect on *Mycobacterium tuberculosis* he con-



siders the therapy worthy of extended trial. [Those acquainted with the extravagant claims made for previous "cures" in leprosy will be disappointed with the absence of controls, the brevity of the observation period (only 4 months), and the inadequate accounts of the cases treated and the methods of assessing results. Nevertheless most encouraging reports have recently been published on the effect of the thiosemicarbazones in experimental and human tuberculosis. In Germany, Domagk has found that its action compares favourably with that of streptomycin and *p*-aminosalicylic acid in the laboratory. Mertens and Bunge reviewed its use in over 10,000 cases of human tuberculosis in Germany and give a very favourable report. Among toxic effects they mention gastric irritation, encephalopathy, exanthemata, anaemia, and rarely agranulocytosis. All are reversible, they say, and may be traced to overdosage. Although American reports are not so optimistic as the German reports, they are favourable enough to reinforce the author's plea for an extended field trial of thiosemicarbazone in the treatment of leprosy.]

William Hughes

### 389. Pulmonary Involvement in Typhoid and Paratyphoid Fevers

F. A. NEVA. *Annals of Internal Medicine* [Ann. intern. Med.] 33, 83-99, July, 1950. 8 figs., 27 refs.

The occurrence of pulmonary complications in typhoid and paratyphoid fever has been stressed in orthodox textbooks of medicine since the early editions of Osler. The present review of 80 cases of typhoid and paratyphoid infection with lesions in the lungs varying from mild bronchitis to fulminating bronchopneumonia in a very large proportion is typical of many previous reports, but no real explanation has been given of the selective affinity of the bacteria concerned for pulmonary tissue. The author believes that there is possibly some direct allergic activity, or more probably a direct specific toxic action upon pulmonary epithelium and its cilia.

G. F. Walker

### 390. A Statistical Study of 140 Cases of Typhoid and Paratyphoid Fever Treated with Chloramphenicol. (Sur une statistique de 140 cas de fièvre typho-paratyphiques traitées par la chloromycétine)

J. LONGCHAMPT and J. CARBONEL. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris* [Bull. Soc. méd. Hôp. Paris] 66, 1248-1252, July 7, 1950.

During an epidemic in the south of France 123 cases of typhoid fever and 17 of paratyphoid B (34 in men, 75 in women, and 31 in children) were treated with chloramphenicol with but one death; of 106 patients treated at the same time without chloramphenicol, 8 died. Dosage varied greatly and in some cases, owing to shortage of the drug, the total dose had to be limited to 20 g. Nevertheless, results were uniformly impressive; temperature and pulse rate fell to normal in from 2 to 6 days, symptoms rapidly subsided, and side-effects were unimportant. Diarrhoea was not controlled by chloramphenicol alone. About 20% of cases relapsed, but responded to a second course of the drug. Relapse was

ascribed to insufficient dosage or duration of treatment, or to commencement of therapy late in the disease. The authors are now of the opinion [expressed by others before them] that successful treatment of typhoid fever with chloramphenicol depends on prolonged administration rather than on high dosage; hence they advise giving 2 to 3 g. daily for 10 days, followed by decreasing doses for another 10 days to a total of 30 g.

D. Preiskel

### 391. Synthetic and Fermentation Type Chloramphenicol (Chloromycetin) in Typhoid Fever: Prevention of Relapses by Adequate Treatment

J. E. SMADEL, C. A. BAILEY, and R. LEWTHWAITE. *Annals of Internal Medicine* [Ann. intern. Med.] 33, 1-17, July, 1950. 4 figs., 16 refs.

A continuation of the studies on the use of chloramphenicol ("chloromycetin") in the treatment of patients with typhoid fever indicates that the synthetic form of the drug is as efficacious as the natural antibiotic obtained by the fermentation process from *Streptomyces venezuelae*. The same total amounts of either type drug are equally effective when given in divided doses at 2 to 6-hour intervals or in larger doses once or twice daily.

There was a definite relationship between the duration of chloramphenicol treatment and the occurrence of relapses in typhoid fever. Slightly more than half of the patients who were treated for 8 days or less had a recrudescence of the disease which began about 10 days after treatment was stopped. No relapses occurred in the groups of patients treated for longer periods of time. The present data suggest that a 14-day period of treatment is sufficient to prevent relapses. In spite of the dramatic therapeutic effectiveness in patients with typhoid fever, serious complications such as intestinal hemorrhage and perforation may be expected in treated patients since the stage is generally set for such developments before therapy is instituted and time is required for the healing of the typhoidal lesion of the intestine. In the present group of 23 patients, 2 had hemorrhage sufficiently severe to produce shock. Two other patients suffered intestinal perforation; the course in one of these was further complicated by severe hemorrhage and the disease terminated fatally. Neither of the patients with perforation was given surgical treatment; chloramphenicol therapy controlled or suppressed the usual signs of generalized peritonitis.

On the basis of the present observations, it would appear that the adequate treatment of typhoid fever in the adult consists of an initial oral dose of 3.0 to 4.0 g. of chloramphenicol, followed by 1.5 g. oral doses given every 12 hours during the febrile period and by single daily 1.5 g. doses for 7 days; thereafter the dose may be reduced to a single 1.0 g. dose and continued until the 14th day of antibiotic therapy, after which the drug may be discontinued. Particular attention should be given to the recognition of intestinal perforation in treated patients since the classical signs of this development with the ensuing generalized peritonitis may be partially masked by the antibacterial effect of chloramphenicol.—[Authors' summary.]

### 392. Observations on the Development of Rheumatic Fever and Glomerulonephritis in Cases of Scarlet Fever Treated with Penicillin

L. WEINSTEIN, L. BACHRACH, and N. H. BOYER. *New England Journal of Medicine* [New Engl. J. Med.] **242**, 1002-1010, June 29, 1950. 21 refs.

A series of 167 cases of scarlet fever were treated with penicillin; the majority of patients received parenteral injections (15,000 units) every 3 hours for 10 days. Twelve patients developed what were considered to be manifestations of rheumatism, and 6 glomerulonephritis.

In assessing rheumatism attention was paid to such matters as latent period, fever, arthralgia, appearance of cardiac murmurs, electrocardiographic changes, and erythrocyte sedimentation rate (E.S.R.). [From the published facts it is impossible to adduce how the cases were distributed in respect of these factors, so that it is difficult to sort out the material. Thus in one paragraph the average latent period is given as 9.2 days; later it is stated that "in the other 12, joint manifestations did not appear until at least 9 days after the onset of sore throat". Yet only 4 of the latter cases were classified as cases of rheumatic fever.] There is a lengthy discussion of the significance of electrocardiographic changes. Most attention was paid to the P-R and Q-T interval; the former was prolonged in 11 and the latter in the same number. However, these changes were not in the same patients, nor were they necessarily noted in simultaneous records. In only one patient was the E.S.R. increased at the time when rheumatic activity was thought to be present.

All 6 patients with nephritis showed albuminuria, casts in the urine, and haematuria after a latent period of 18 to 25 days. Three patients had fever, and in 3 (not necessarily the same) the E.S.R. was raised at the time of the development of urinary abnormalities. In only one patient did the authors find actual clinical evidence of nephritis.

It is concluded that the administration of penicillin in cases of scarlet fever does not prevent the development of rheumatism or nephritis; since the complication rates are similar to those encountered before the use of penicillin, it is considered that the possibility of the occurrence of these complications is not reduced by such a form of treatment.

[In the same issue there is a leading article which discusses (without adding much light) the conflicting results obtained by different investigators, particularly contrasting the above negative report with the good results obtained by Denny *et al.* (*J. Amer. med. Ass.*, 1950, **143**, 151) in a large-scale study on Air Force personnel. The latter investigation was well controlled and deserves particular emphasis for that reason. The abstracter wonders, however, how much reliance is to be placed on the prevailing custom of diagnosing rheumatic fever on the strength of minimal changes found in serial electrocardiographic tracings. Has such a study been made upon presumably normal persons? The abstracter suspects that such a study would show that such "abnormalities" occurred with a frequency not differing greatly from that reported in the above paper.]

T. Anderson

### 393. Meningitis due to Simultaneous Double Infections in Children

E. B. VADEN, E. C. RICE, and V. STADNICHENKO. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 1402-1404, Aug. 19, 1950. 13 refs.

From January, 1947, to July, 1949, 10 cases of meningitis due to simultaneous infection with two organisms were observed in the Children's Hospital, Washington. In 9 cases *Haemophilus influenzae* was one of the organisms, being associated with meningococci (4 cases), streptococci (3), and pneumococci (2). In one patient the infection was due to pneumococcus and *Bacterium coli*. In all but one of the patients both organisms were isolated in culture from spinal fluid obtained at the first puncture. All the patients were under 5 years of age, 5 being infants under 1 year. Treatment was with sulphadiazine and penicillin, 7 of the patients receiving streptomycin in addition in usually accepted doses. All the patients recovered.

The authors state that they have been able to find reports of only 13 cases of double meningeal infection in the literature, but as their 10 cases account for 8% of all cases of purulent meningitis admitted to the Children's Hospital over a period of 30 months, this phenomenon may perhaps be more common than has hitherto been recognized. They suggest that, pending bacteriological reports, all cases of purulent meningitis should be treated on the assumption that a double infection may be present.

Joseph Ellison

### 394. Chloramphenicol in the Treatment of *Haemophilus influenzae* Meningitis

G. W. PRATHER and M. H. D. SMITH. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **143**, 1405-1406, Aug. 19, 1950. 1 fig., 11 refs.

From the Charity Hospital, New Orleans, the authors report the treatment with chloramphenicol of 15 consecutive, unselected cases of *Haemophilus influenzae* meningitis. Of these 15 patients, 8 were infants under one year. In every case *H. influenzae* type-B organisms were recovered in culture from the spinal fluid, but fluid from a second puncture performed within an average interval of 21 hours was sterile. All the patients recovered, no toxic effects attributable to the drug being observed. On the basis of this experience the authors recommend immediate doses of between 50 and 100 mg. per kg. body weight by mouth or stomach-tube, followed by 250 mg. 8-hourly for 5 or more days irrespective of body weight. They consider this method of treatment to be more satisfactory than any other known to them.

Joseph Ellison

### 395. Influenzal Meningitis Treated with Chloromycetin. A Preliminary Report

R. W. CARABELLE, D. D. MITCHELL, and G. W. SALMON. *Journal of Pediatrics* [*J. Pediat.*] **37**, 37-41, July, 1950. 5 figs., 10 refs.

Chloramphenicol ("chloromycetin") was successfully used by the authors in the treatment of an infant suffering from influenzal meningitis which had not responded to streptomycin and sulphadiazine. They then treated

4 other infants under 2 years of age with chloramphenicol alone. The dose aimed at was 60 mg. per kg. body weight every 24 hours. The initial doses were given by gavage to prevent vomiting, and after 36 to 48 hours the drug was given orally in "amphojel" or jelly.

Case reports are given which show the rapid improvement obtained. There were no residua at the time of discharge, but further observation of the patients is required to detect possible sequelae. In 3 of the infants upper respiratory infections developed while they were under treatment, but these cleared up in a few days without additional therapy. However, the authors are of the opinion that for the management of severe influenzal meningitis other therapeutic agents are required in combination with chloramphenicol. *B. S. P. Gurney*

**396. Inapparent Salmonella Infections in Hospitals**

J. Felsen, A. J. Weil, and W. Wolarsky. *Journal of the American Medical Association* [J. Amer. med. Ass.] **143**, 1135-1138, July 29, 1950. 9 refs.

This paper describes the measures taken for the prevention of outbreaks of *Salmonella* infection at the Bronx Hospital, New York. Since 1934 routine faecal cultures have been examined for salmonellae, on initial employment and monthly thereafter, from the hospital's food-handling staff, dietetic staff, and nurses on duty in the children's wards. More recently the faeces of all obstetric patients have been similarly examined on admission. A considerable number of carriers of salmonellae have been detected in this way before outbreaks have occurred. During 1949 approximately 2,000 faecal cultures were made and 5 inapparent *Salmonella* infections were revealed, the species concerned being *Salm. montevideo* (one nurse), *Salm. tennessee* (one cook, one food-server, one formula-room employee), and *Salm. typhi* (one parturient mother); in addition, *Salm. oranienburg* was isolated from pus from a perirectal abscess and from the faeces of one hospital patient. The authors recommend the appointment of an epidemiologist to the staff of every hospital. *Joyce Wright*

**397. Chloramphenicol (Chloromycetin) Therapy in Shigella Enteritis**

S. Ross, F. G. Burke, E. C. Rice, J. A. Washington, and S. Stevens. *Journal of the American Medical Association* [J. Amer. med. Ass.] **143**, 1459-1460, Aug. 26, 1950. 3 refs.

Chloramphenicol has been used in the treatment of 35 children, aged between 3 months and 7 years, suffering from bacterial dysentery (due in 33 cases to *Salmonella sonnei* and in 2 to *Salm. flexneri*). Tests of sensitivity to the drug were made on the isolated organisms, which all proved sensitive to 5 µg. per ml. or less. Each case was confirmed bacteriologically before treatment was started, and daily stool cultures were made throughout the stay in hospital. In general, the dosage employed was 250 mg. 4-hourly for about 8 days. In all but 2 of the 35 cases stool cultures became negative within 12 to 36 hours of starting treatment. Of the other 2 the stools in one became negative in 48 hours, and in the other in 6 days, but relapse occurred later. This patient was

treated again with 500 mg. of chloramphenicol 4-hourly for 10 days and recovered completely. Clinically, the disease subsided *pari passu* with the bacteriological findings, much improvement usually being seen within the first 24 hours, though extensive fluid therapy was needed in a few cases, mostly in infants. Diarrhoea subsided within 3 days and all the patients were discharged cured after 8 consecutive negative bacteriological reports on the stools. Side-actions seem to have been chiefly due to the bitter taste of the drug, many of the patients being too young to take the capsule intact. Anorexia and vomiting were observed in a few cases, but were only transitory. In 4 female patients vulvovaginitis was observed about 5 days after starting treatment, but it cleared up when administration of the drug was stopped.

Comparison is made with the results of treatment with other drugs. It was found that sulphadiazine, streptomycin, polymyxin B, and chloramphenicol all produced negative bacteriological results within 2 days, the average figures being 2.0, 1.6, 1.9, and 0.76 days respectively, and the differences being statistically insignificant. There are, therefore, four drugs now available which may be expected to clear up bacterial dysentery quickly and completely.

*Reginald St. A. Heathcote*

**398. Chloramphenicol in the Treatment of the Acute Manifestations of Brucellosis**

V. Knight, F. Ruiz-Sanchez, and W. McDermott. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] **219**, 627-638, June, 1950. 6 figs., 8 refs.

The authors studied 13 patients suffering from brucellosis who were treated with chloramphenicol. In general, the dosage was 50 to 100 mg. per kg. daily during the febrile period, followed by 25 mg. per kg. daily up to a total period of 6 to 10 days. In 5 patients there was a rapid subsidence of fever and they remained well. There was an early improvement in symptoms in 2 patients, both with bacteraemia and both severely ill, but fever continued after chloramphenicol was stopped. In one of these 2 cases a second course of treatment instituted immediately resulted in rapid and apparently permanent improvement. In the other there was a long period of low-grade fever; later there was a prompt and beneficial response to a second course of the drug. Relapses occurred in 6 cases within 1 to 8 weeks of the end of the treatment. These patients had received the drug for periods ranging from 6 to 10 days. In 3 of them the relapses were mild, but in the other 3 the symptoms were fairly severe. In all of these patients the infection was adequately controlled by a further course of treatment. Symptoms and signs of a drug-induced exacerbation developed in 5 patients during the first or second day of treatment, but in no case did this cause alarm. No other serious toxic effects were encountered.

The uniform manner in which all patients improved after treatment was started, even though cure was not established, was a striking feature and was thought to indicate a beneficial therapeutic action. The authors considered that the high relapse rate was due to the short period of treatment and that a more prolonged course



(even up to 4 to 6 weeks) might be justified. For the average adult the suggested optimum dosage is about 6 g. per day. A comparison between the temperature charts of 11 patients treated with aureomycin and the temperature charts of those in the present series given chloramphenicol does not reveal any great difference in the efficacy of the two drugs.

T. Anderson

### TUBERCULOSIS

#### 399. *p*-Anisaldehyde-thiosemicarbazone in Treatment of Experimental Murine Tuberculosis

M. M. STEINBACH and H. BAKER. *Proceedings of the Society for Experimental Biology and Medicine* [Proc. Soc. exp. Biol., N.Y.] **74**, 595-596, July, 1950. 10 refs.

*para*-Anisaldehyde thiosemicarbazone at a concentration of 1 µg. per 100 ml. in Dubos medium prevented the growth *in vitro* of the H37 Rv and B1 strains of *Mycobacterium tuberculosis*. [In the summary, the inhibitory concentration of drug is given as 1 mg. per 100 ml.]

When the drug was administered in the diet at a concentration of 1% to mice infected by intravenous injection of a culture of the H37 Rv strain, the mice were prevented from dying of gross pulmonary tuberculosis. After 30 days, when all the infected control mice were dead, treated animals showed no gross pulmonary or other tuberculous lesions, but the spleen was enlarged. The findings in animals killed 75 days after inoculation were similar.

L. G. Goodwin

#### 400. Significance of Changes in the Content of Serum Polysaccharide during Sensitization and Development of Tuberculosis

F. B. SEIBERT and M. V. SEIBERT. *American Review of Tuberculosis* [Amer. Rev. Tuberc.] **62**, 67-76, July, 1950. 4 figs., 6 refs.

While studying the immunizing properties of various tuberculin-protein fractions in comparison with B.C.G. in rabbits, the authors investigated the polysaccharide content of serum during the immunization process and subsequent virulent infection. The tryptophan-acid (T.A.) method was used for polysaccharide determination and the relative values expressed in terms of the Klett readings. The Klett reading of 80 seemed to be a critical value. After this was reached the rabbits began to lose weight, and died after an average of 105 days, irrespective of treatment before virulent infection.

Sensitization with two tuberculin-protein fractions, A and C, prepared from unheated tuberculin and differing in electrophoretic mobility, tuberculin potency, and capacity for producing anaphylactic reactions, led to significant increase in T.A. values during the sensitization process. This was comparable to the rise observed during the course of tuberculous infection in rabbits not pre-treated. The rise was more marked with fraction A, and this fraction also produced larger Arthus reactions. No significant increase in T.A. values was found in rabbits or human subjects after sensitization with B.C.G. vaccine. Subsequent virulent infection

of the animals sensitized with the tuberculin-protein fractions led to further rapid increase in T.A. values and death. In rabbits immunized with B.C.G., T.A. values rose much more slowly after virulent infection, and the critical T.A. value was less frequently, and much more slowly, reached. When, however, it was reached, death ensued in much the same time as in the other groups. It is concluded that the critical T.A. Klett reading of 80 may be of significant prognostic value in experimental tuberculosis of the rabbit.

E. Nassau

#### 401. Vaccination with Freeze-dried BCG. Preliminary Clinical Reports

F. VAN DEINSE and F. SÉNÉCHAL. *Tubercle* [Tubercle] **31**, 185-189, Aug., 1950.

Reports from various workers in France, the Belgian Congo, the Philippines, Singapore, and Turkey, collected by the authors at the Pasteur Institute in Paris, indicate that the concentrated freeze-dried B.C.G. vaccine prepared by the Institute has kept its potency under varying climatic conditions and produces allergy as efficiently as fresh B.C.G. vaccine. Suspended in saline, the freeze-dried vaccine can be equally well applied by the multiple puncture technique, by scarification, or, appropriately diluted, by intracutaneous inoculation.

E. Nassau

#### 402. Psychological Factors in the Pathogenesis of Tuberculosis. (Psychische Faktoren bei der Pathogenese der Tuberkulose)

H. HUEBSCHMANN. *Zeitschrift für Tuberkulose* [Z. Tuberk.] **95**, 156-166, 1950. 18 refs.

Infection does not necessarily imply disease. The author poses the following questions: (1) Why do the majority of those infected not develop clinical disease? (2) In those who do, why does it happen and why at the particular time the disease becomes manifest? [In tuberculosis this may be soon or a long time after infection has taken place.] (3) Are the ups and downs, the tendency to healing or to exacerbation, merely dependent on local conditions, on the amount and "virulence" of the germs, and on exogenous physical factors? The conventional concept of disease and pathogenesis, based on pathology and bacteriology, that is, orthodox clinical medicine, fails to supply satisfactory answers to these vital questions.

Only by re-introducing the subject [as a third force] into pathology can the disease process be properly understood. The "subject", that is, the patient's personality, determines the individual reaction to infection, and indeed to the environment as a whole. The psyche in its unconscious manifestations is this "third force" which, through the central nervous system (diencephalon) and the autonomic nervous system, controls such vital functions as the circulation and hormonal and haematological functions on which the tissue reaction to trauma and infection depends.

The detailed analysis of 2 case histories shows how the emotional tension resulting from the repression of a conflict may provide the source of that energy which can

change the patient's "disposition" and might seriously upset biological balance. The cases illustrate how a psychosomatic approach to medicine greatly contributes to understanding of disease and recovery.

E. G. W. Hoffstaedt

**403. Exogenous Reinfection in Cured Tuberculosis. (Comparative Incidence of Relapse in Tuberculous Physicians Working in Sanatoria and Elsewhere.)** (La réinfection exogène chez le tuberculeux guéri. (Fréquence comparée des rechutes chez les médecins anciens tuberculeux exerçant et n'exerçant pas la phthisiologie)) G. CANETTI and M. ROBERT. *Revue de la Tuberculose* [Rev. Tuberc., Paris] **14**, 451-457, 1950. 1 ref.

The authors have studied the incidence of relapse in doctors who contracted tuberculosis while medical students, and who were treated at the students' sanatorium at St. Hilaire. The 263 patients studied had all been discharged from sanatoria as recovered, patients found suffering from reactivation of lesions within 2 years of discharge having been excluded from the analysis. After qualification 141 had taken up tuberculosis work (104 of them as physicians in sanatoria); the other 122 had gone into general practice or specialities other than tuberculosis. The two groups were comparable in social background, in the type of original disease, and in the mean period of observation—7.1 years in one group, 6.6 in the other.

Relapses occurred in 35 (24.8%) of the 141 doctors working in contact with tuberculosis, and in 14 (11.5%) of the 122 other doctors. The annual relapse rate was 3.5% in the first group, 1.75% in the other. Since the two groups of doctors are in all other respects comparable, the authors conclude that the additional relapses in doctors working in tuberculosis were due to fresh exogenous reinfection. They discuss the special risks of reinfection which are associated with bronchoscopy, radioscopy, and the performance of pneumothorax refills, and make strong recommendations concerning prophylactic measures which can easily be applied to reduce these risks.

M. Daniels

**404. Nerve Dysfunction in Chronic Disseminated Forms of Pulmonary Tuberculosis.** (О нервных дисфункциях при хронических диссеминированных формах туберкулеза легких)

L. A. SHASS. *Проблемы Туберкулеза* [Probl. Tuberk.] No. 4, 26-31, July-Aug., 1950.

The author deals with the influence of the nervous system on the course of tuberculosis. It is generally known that tuberculous patients suffer from changes in temperament, including increased irritability, sensitivity, and other signs of nervous dysfunction. The vegetative part of the nervous system is also affected at times. The condition of the nervous system was studied in 88 cases of disseminated forms of tuberculosis (79 men and 9 women) and it was thought that in this series nervous dysfunction occurred twice as frequently as in localized forms of tuberculosis. In most cases there were signs of neurasthenia with emotional changes and increased irritability. Many patients suffered from

nervous headaches and vertigo. Pains in the chest, neuralgia, and brachial and sciatic neuritis were also observed in many cases. The author tries to show that it is important that tuberculous patients should be treated by psychiatrists as well as clinicians, since this dysfunction often coincides with exacerbations of the disease.

H. W. Swann

**405. Arterial Oxygen Saturation in Pulmonary Tuberculosis before and after Thoracoplasty. A Clinical Investigation.** [In English]

T. W. AAS. *Acta Tuberculosea Scandinavica* [Acta tuberc. scand.] **24**, 365-387, 1950. 15 figs., 29 refs.

The author presents the results of estimations of arterial oxygen saturation by the Van Slyke method in a series of 4 groups of 4 or 5 patients with pulmonary tuberculosis, for which they received treatment by artificial pneumothorax, phrenic nerve interruption, or apical thoracoplasty. None of the series is large enough to draw satisfactory conclusions. [If they are to be of any value, estimations of disturbance of pulmonary physiology must include measurement of alveolar CO<sub>2</sub> tension as well as blood pH.] Patients who had not had a thoracoplasty were grouped according to their arterial oxygen saturation, and an attempt was made at correlation with the clinical and radiological findings. In 5 patients with an arterial oxygen saturation of less than 90 volumes per 100 ml., the lungs and pleura were extensively involved and diaphragmatic movement was somewhat impaired. Estimations of arterial oxygen saturation, sometimes before and usually 1 day and 5 to 6 days after operation, were made on 10 patients undergoing thoracoplasty and 2 undergoing extrapleural pneumolysis. The chief value of these estimations is to emphasize the need for maintaining adequate pulmonary ventilation, by bronchoscopic aspiration if necessary or by the removal of intrapleural collections of fluid, and a suitable circulating blood volume with as high an erythrocyte content as possible. When these factors have been controlled, oxygen therapy is likely to be most efficacious, and the risks to the cerebral mechanism from oxygen deficiency are reduced. In most cases the author found that there was but slight post-operative reaction and no anoxaemia following apical thoracoplasty. [Of the 29 references in the bibliography only 2 are cited in the text.]

Kenneth Marsh

**406. Domiciliary Treatment of Pulmonary Tuberculosis with Sodium para-Aminosalicylate**

D. L. PUGH, E. R. JONES, and W. J. MARTIN. *Lancet* [Lancet] **2**, 92-97, July 15, 1950. 31 refs.

The authors describe the use of sodium *p*-aminosalicylate (PAS) in the domiciliary treatment of 50 patients with pulmonary tuberculosis, of whom 23 were treated for 12 weeks and 27 for 6 weeks, 106 patients with similar lesions and of the same economic status being used as controls. A dose of 3 g. of PAS was given six times daily in a mixture with syrup of orange, and this was found to be well tolerated. Of the 50 patients, 26 experienced mild gastro-intestinal disturbance, but it responded to "benadryl" (diphenhydramine) and in no

case was it found necessary to abandon the treatment. One patient developed symptoms of acquired idiosyncrasy, with pyrexia, headache, sweats, and an erythematous rash. Desensitization was satisfactorily carried out with progressively increasing doses, and the course was completed. The level of PAS in the blood was estimated by means of Ehrlich's reagent [though no figures are quoted]. PAS-sensitivity tests of tubercle bacilli grown from the sputum were performed and indicated that there is normally a wide variation in sensitivity of the bacilli to the drug. A resistant strain of the tubercle bacillus was found to have developed in one case.

The majority of patients in both treated and control groups showed improvement, but the authors consider that there is a definite place for the use of sodium *p*-aminosalicylate as part of a planned treatment scheme.

R. H. J. Fanthorpe

**407. The Employment of Vitamin D<sub>2</sub> in Pulmonary Tuberculosis.** (Über die Vitamin-D<sub>2</sub>-Anwendung bei Lungentuberkulosen)

F. SEEBER. *Zeitschrift für Tuberkulose* [Z. Tuberk.] **95**, 151-155, 1950. 17 refs.

Of 28 cases of pulmonary tuberculosis treated with small doses of vitamin D<sub>2</sub>, 12 showed definite improvement as regards general condition, temperature, sedimentation rate and blood count, sputum, and radiological and clinical findings. The improvement exceeded what could be expected from routine treatment. In the remaining 16 cases no change could be ascribed to the vitamin treatment. With a daily dose of 0.75 mg. (30,000 i.u.) and up to a total dose of 150 mg. no toxic side-effects were seen. [The assessment of the results of treatment is critical; no theory of the specific action of the vitamin is offered.]

E. G. W. Hoffstaedt

**408. Vitamin D<sub>2</sub> Alone and Combined with "TB I/698" in the Treatment of Pulmonary Tuberculosis.** (Vitamin D<sub>2</sub> allein und in Kombination mit TB. I/698 bei der Behandlung der Lungentuberkulose)

W. GERECKE. *Zeitschrift für Tuberkulose* [Z. Tuberk.] **95**, 182-187, 1950. 8 figs.

Whereas in 81 patients with pulmonary tuberculosis 11 months of treatment with vitamin D<sub>2</sub> (1 mg. per day) had no influence on the course of the disease, a combination of the vitamin with "TB I/698" (thiosemicarbazone) gave some good results. The results of this combined treatment were better than with TB I/698 alone. Though, according to Raab, addition of vitamin D<sub>2</sub> to culture media in a strength of 50 i.u. per ml. of medium prevents the growth of *Mycobacterium tuberculosis*, the therapeutic concentration of the vitamin is not likely to have a specific bacteriostatic action. A non-specific anti-allergic effect is assumed which, possibly via the autonomous nervous system, improves conditions for the specific action of thiosemicarbazone. Vitamin D<sub>2</sub> itself had no apparent additional effect when given with collapse treatment.

Four cases are described in detail and illustrated by radiographs.

E. G. W. Hoffstaedt

**409. Cases of Advanced Childhood Pulmonary Tuberculosis Treated with Streptomycin Aerosol**

J. B. MILLER, H. A. ABRAMSON, and B. RATNER. *Quarterly Bulletin of Sea View Hospital* [Quart. Bull. Sea View Hosp.] **11**, 102-115, July, 1950. 36 refs.

This paper reports a study of the effectiveness of large doses of streptomycin, in a special diluent, given as an aerosol. The streptomycin was dissolved in water which had been made alkaline (pH 8.0) and contained a detergent ("triton A20", 0.1%) and glycerin (2%). The patients received 1 g. of streptomycin in 5 ml. of solvent twice daily for 3 to 6 months by the aerosol method, oxygen and a De Vilbiss nebulizer being used. Three inches of rubber tubing formed a mouthpiece to deliver the aerosol to the back of the mouth, the nose being occluded. For children who could not co-operate and use the usual Y-tube, a face hood made of cellophane was found to be the best apparatus. This treatment was given to 12 children aged from 8 months to 15 years; 9 of these with extensive lung disease, including one with miliary tuberculosis, responded well and became clinically healed. There was little response in 3 with collapse of the whole or part of a lung. There were no toxic effects and no increase in streptomycin resistance during treatment.

[The results in 9 cases in which otherwise the prognosis would have been poor fully justify the authors' cautious conclusion that "further study of the value of this technique is indicated".]

L. M. Franklin

**410. Treatment of Cavitating Pulmonary Tuberculosis with Nitrogen Mustard and Streptomycin.** (Próby leczenia serowatojamistej gruźlicy płuc nitrogranulogenem i streptomycyną)

J. ALEKSANDROWICZ. *Polski Tygodnik Lekarski* [Polsk. Tyg. lek.] **5**, 686-699, May 2, 1950. 8 figs., 29 refs.

In this article from a Polish medical centre the author describes how the effect of nitrogen mustard on pulmonary tuberculosis was discovered by its accidental administration in a case in which a diagnosis of neoplasm was later changed to one of pulmonary tuberculosis. The rationale of this novel therapeutic measure is discussed, and it is pointed out that the acceleration of the "cicatization process" caused by nitrogen mustard may be usefully combined with the antibiotic activity of streptomycin and sodium *p*-aminosalicylate. The dose of nitrogen mustard employed is 0.005 to 0.03 mg. per kg. body weight for 3 to 8 days repeated at intervals for from 3 to 5 weeks.

Five series of cases were studied. The first series consisted of 9 cases with severe pulmonary lesions and 6 cases with "mild" lesions, all treated with nitrogen mustard for from 12 to 24 months. There were no satisfactory results in the former group, but in the latter group of six "mild" cases, four were healed and one showed striking improvement.

The second series of 15 patients with advanced lesions had treatment with nitrogen mustard for from 3 to 12 months; in 5 cases improvement was marked, in 5 cases it was moderate, and in 2 it was slight. The third series consisted of 15 cases already treated for 3 months with



streptomycin without improvement. The results here were identical with those in the second series. A fourth series of 12 cases with advanced lesions were treated with nitrogen mustard and with 0.5 g. streptomycin daily up to a total of 10 g., together with 150 g. of sodium *p*-aminosalicylate. In 7 cases improvement was definite and in one case slight.

A fifth series was studied as a control, physiological saline being given instead of nitrogen mustard, but therapy being otherwise identical with that in the fourth series. No case in this last series showed any marked degree of improvement.

I. McLean-Baird

#### 411. Treatment of Endobronchial Tuberculosis with Streptomycin

E. D. ERMAN. *Journal of Thoracic Surgery* [J. thorac. Surg.] 20, 52-54, July, 1950. 9 refs.

Among 1,108 patients with clinical pulmonary tuberculosis who were examined bronchoscopically at Fitzsimons General Hospital, Denver, Colorado, 92 cases of endobronchial tuberculosis were found. Of these, 49 were kept under observation during treatment with 1 g. of streptomycin daily. Complete healing without fibrostenosis occurred in all 23 patients with hyperplastic endobronchial tuberculosis in an average time of 42 days, while in all 15 patients with submucosal lesions the condition healed completely in the same average time. Out of 11 patients with ulcerative endobronchial tuberculosis the lesions healed without fibrostenosis in all but 3 cases, the average time taken for healing being slightly longer than in the other groups.

Kenneth Marsh

#### 412. Effect of Triton A-20 and pH Value on the Streptomycin Sensitivity of a Resistant Strain of *M. tuberculosis*

C. HURWITZ and J. B. MILLER. *American Review of Tuberculosis* [Amer. Rev. Tuberc.] 62, 91-98, July, 1950. 18 refs.

The effects of "triton A-20", a wetting agent (an aryl-alkyl polyether alcohol), and of the pH of the medium on the streptomycin-sensitivity of a resistant strain of *Mycobacterium tuberculosis* were studied in connexion with an investigation into the value of streptomycin aerosol treatment in pulmonary tuberculosis. The aerosol employed contained streptomycin in saline, buffered to an alkaline pH, and triton A-20. The idea was to enhance the action of streptomycin by using it in an alkaline medium and rendering it lipoid-soluble.

A modified Williston-Youmans liquid medium containing varying amounts of triton A-20, but no bovine albumin or glucose, was used. Four lots of the medium, containing 0.05%, 0.1%, 0.5%, and 1% triton A-20, were each further divided and adjusted to pH values of 6, 6.5, 7, 7.4, and 8. Streptomycin in amounts of 0, 1, 10, 100, 500, and 1,000 µg. per ml. was added to each lot of medium. A sensitive strain of *Myco. tuberculosis* failed to grow in any of the media containing 1 µg. of streptomycin or in the control media at pH 8. Growth of the resistant strain was retarded by triton A-20 at concentrations below 0.10%, was at its maximum at 0.10%, and decreased again with higher concentrations.

At an initial pH value of 7 the tubercle bacilli grew in 10 but not in 100 µg. of streptomycin per ml. of medium. At pH 6.5 they grew in 100 µg., at pH 6 growth occurred in 1,000 µg., but optimum growth was obtained with 100 and 500 µg. per ml. of medium. Triton A-20 became increasingly inhibitory to tubercle bacilli as the pH was increased above 7; it had no influence on the streptomycin-sensitivity of the resistant strain. The possible use of an alkaline aerosol of triton A-20, with or without streptomycin, in the treatment of pulmonary tuberculosis is discussed.

E. Nassau

#### 413. A Comparative Study of Susceptibility of Tubercle Bacillus (H37 Rv) to Aureomycin, Streptomycin, and para-Aminosalicylic Acid

M. M. STEINBACH, H. BAKER, and C. J. DUCA. *Proceedings of the Society for Experimental Biology and Medicine* [Proc. Soc. exp. Biol., N.Y.] 74, 596-598, July, 1950. 6 refs.

Aureomycin in a concentration of 1 µg. per ml. in Dubos medium inhibited the growth of *Myobacterium tuberculosis* H37 Rv. The concentration of aureomycin was maintained by adding suitable amounts every 24 hours to replace drug lost by "deterioration". Growth was also inhibited by streptomycin at a concentration of 1 µg. per ml., and by *p*-aminosalicylate at a concentration of 4 µg. per ml.

Groups of mice infected by the intravenous injection of tubercle bacilli received subcutaneous injections every 12 hours of 0.25 ml. of solutions of aureomycin containing 1,000 or 5,000 µg. per ml. Other groups were given subcutaneous injections of a solution of streptomycin containing 1,000 µg. per ml., or were given 1.5% of *p*-aminosalicylic acid in the diet. Necropsy showed that streptomycin and *p*-aminosalicylic acid had measurable effects upon the development of tuberculous lesions, but that aureomycin was quite inactive, even when given in high doses.

L. G. Goodwin

#### 414. Comparison of the Radiological and Histological Findings in Cases of Acute Miliary Tuberculosis from a Primary Infection Treated with Streptomycin. (Aspetti e raffronti radiologici ed anatomo-istologici nelle miliari acute clinicamente primitive del ciclo primario trattate con streptomicina)

A. BLASI, M. RAMAGLIA, and V. VERGA. *Archivio di Tisiologia* [Arch. Tisiol.] 5, 363-404, May, 1950. 27 figs., 34 refs.

The most significant changes caused by treatment with streptomycin occur in cases of acute miliary tuberculosis. The authors report on a series of 7 children suffering from this disease. All these patients were treated with streptomycin, and treatment began in the initial stages of the disease. All the patients died with involvement of the meninges. This complication developed at various times after the commencement of treatment. In all these cases acute miliary tuberculosis followed a primary lesion. The survival time varied from 2 to 8 months. Tuberculous meningitis developed 1 to 6 months after the beginning of the treatment with streptomycin and was always secondary to a pulmonary condition, which almost

always showed some degree of improvement under this treatment. The syndrome of meningitis was completely independent of the condition in the lungs, whether or not the latter improved clinically and radiologically. These observations are identical with those of other authors.

In the cases observed by the authors streptomycin changed the usual course of the disease only partially; treatment influenced the primary lung condition beneficially and prevented temporarily the dissemination of bacilli. However, subsequent bacteraemia could not be prevented, and the meninges were soon affected. Most probably those foci act as disseminating centres which would act as such if no streptomycin were administered.

Radiological appearances vary from subject to subject. In some cases the radiological appearances in the lungs do not alter during the course of the disease and present the widespread "miliary" picture. In other cases appearances in lungs do not show any quantitative change under streptomycin treatment, but individual foci become better defined and denser. In another group of cases, soon after commencement of streptomycin treatment, lung fields clear considerably, with better definition and increase in density of the individual foci. In the last group of cases transient and almost complete clearing of the lung fields is followed by rapid deterioration in the radiological appearances. The authors stress the point that only a very small percentage of cases treated with streptomycin show no evidence of radiological improvement. Radiologically there may be apparent complete recovery while histology still reveals the activity of the process. To explain this discrepancy, it must be realized that the miliary tubercle cannot be seen if its diameter is below 0.5 mm. The radiological visibility of the tubercle is associated mainly with the surrounding reaction of the tissues and not with the caseous centre.

From the pathological point of view, cases followed one of the following three courses: (1) Structural changes within foci, and their demarcation. This course was followed by the majority of cases. The caseous centres decreased in size and there was evidence of peripheral cellular reaction, with attempts to form a scar. A clearly demarcated zone surrounded such a healing focus. (2) Structural changes within foci, without tendency to organization. There was complete absence of the caseous centre. The mass of epithelial cells occupied the centre of the focus. There was almost complete absence of giant cells, which appeared only in cases where much regression had taken place. There was a marked accumulation of lymphocytes in the periphery of the lesion, and some of these cells tended to penetrate to its centre. (3) Persistence of the characteristics of the foci. Practically no change in histological appearances followed the administration of streptomycin. The centre of the lesion was caseous, the periphery teemed with lymphocytes. There was no organized tendency to demarcation.

It is not yet possible to state that antibiotic treatment can transform acute miliary tuberculosis into a chronic or more benign process. On the other hand, there is no

doubt that this treatment causes healing of miliary foci. The bacteriostatic action of streptomycin is aided by its dehydrating action, which accelerates the absorption of the caseous centre, but this does not imply complete resolution of the focus.

W. J. Czyzewski

See also Sections Pharmacology and Therapeutics, Abstract 74; Microbiology, Abstracts 163, 170.

*Correction.*—The dose of PAS administered to 23 patients suffering from various forms of tuberculosis (Abstract 1720 in the October issue of this journal) was 15 g. daily given in 3-hourly doses.—EDITOR.

## PROTOZOAL INFECTIONS

### 415. The Effect of Aureomycin on *Entamoeba histolytica* *in vitro*

R. HEWITT, W. WALLACE, and E. WHITE. *Science* [Science] 112, 144–147, Aug. 4, 1950. 6 refs.

The authors describe the effect of aureomycin hydrochloride on *Entamoeba histolytica* *in vitro*, in which they used cultures with a mixed bacterial flora, grown in a medium consisting of liver-infusion agar-slope overlaid with Loeffler–Ringer solution or horse-serum saline and containing rice starch. Tests were carried out by two methods. In one, varying dilutions of the drug were dissolved in the overlay, after which the medium was inoculated with 0.1 ml. of a rich 48-hour culture. At the end of 48 hours at 37° C. the cultures were examined microscopically. Growth of the amoebae was scarce or completely inhibited in dilutions of aureomycin up to 1 in 100,000, but since bacterial growth was also inhibited considerably at high dilutions of the antibiotic and completely prevented at low dilutions, it could not be determined by this method whether aureomycin had any direct effect upon the amoebae.

This element of doubt was excluded in the second method, in which 2-ml. amounts of pooled overlays of 48-hour cultures of amoebae were cultivated in 8 ml. of saline, to which aureomycin was added. After exposure for 10 to 60 minutes, the mixture was repeatedly centrifuged at 2,000 r.p.m. for 3 minutes, decanted, and washed with saline. The sediment containing amoebae was then inoculated on media previously seeded with the original bacterial flora, and the resulting growth of amoebae was recorded after 48 hours' incubation. It was shown that aureomycin had a marked amoebicidal effect in a dilution of 1 in 1,000 and less pronounced effects at 1 in 10,000. In comparison, the amoebicidal action of emetine after contact for 60 minutes at a dilution of 1 in 1,000 was less. It was found that varying the pH between 3.12 and 8.0 made no measurable difference in the effect of these dilutions of aureomycin. Similar tests *in vitro* were made with 1 in 1,000 dilutions of streptomycin, bacitracin, and chloramphenicol, but none of those antibiotics had any measurable effect on *E. histolytica* after exposure for one hour.

It is concluded that although it cannot be inferred from tests *in vitro* that aureomycin has a similar effect in human infections, this is a possibility which must be taken into consideration.

C. A. Hoare

#### 416. Treatment of Amebiasis with Bacitracin and Other Antibiotics

H. MOST, J. W. MILLER, and E. J. GROSSMAN. *American Journal of Tropical Medicine* [Amer. J. trop. Med.] 30, 491-497, July, 1950. 3 refs.

The authors report from New York University on the action of bacitracin, aureomycin, chloramphenicol, and polymyxin B in the treatment of amoebiasis. The series treated with bacitracin consisted of 51 patients, of whom 13 were asymptomatic and 8 moderately or severely ill with demonstrable lesions in the colon. The drug was given orally in doses of 40,000 to 120,000 units daily over periods of 5 to 20 days. In all but 3 cases clinical and parasitological cure was obtained after the first course, but in 14 cases parasitological relapse occurred after a period ranging from 6 to 350 days. Among the 9 out of these 14 patients who had a second course there were 6 relapses, and following a third treatment there were 2 failures out of the 6 cases treated. Clinically, there was early and striking improvement in all the moderate and severe cases. Dysentery disappeared within a few days, amoebae disappeared from the stools, and ulcers healed in 4 to 14 days. One case which had previously resisted treatment with emetine, iodoquinolines, and carbarsone yielded rapidly to bacitracin and, although there was relapse later, a second treatment was successful. The antibiotic does not appear to be absorbed from the gastro-intestinal tract, and no toxic symptoms beyond abdominal distension and a mild diarrhoea were noted. A series of 32 asymptomatic or mildly symptomatic cases were treated with aureomycin, 1 to 2 g. daily in divided doses, for 10 days. There was no response in one severe case, although treatment was continued until 23.25 g. had been given over 9 days. In all the other cases amoebae disappeared from the stools. Only one relapse has been noted so far, but the period of observation has been short in some of the cases. Toxic symptoms included troublesome vomiting and diarrhoea, but recent samples of the drug, given in reduced dosage of 1 g. daily, have been much less toxic. Chloramphenicol and polymyxin B were each tried in 6 cases and failed to effect a cure. Discussing their results the authors point to the lethal action of bacitracin and aureomycin on the intestinal flora—particularly the enterococci and clostridia. They consider that a symbiotic relationship exists between these organisms and *Entamoeba histolytica* and that the elimination of the former alone promotes healing of the intestinal ulcers. In spite of the short periods of observation in these cases it appears that aureomycin will probably be even more effective than bacitracin and the authors advocate the use of one of these antibiotics in conjunction with emetine as a routine addition to therapy.

William Hughes

#### 417. A Study of Sleeping Sickness in an Endemic Area of the Belgian Congo over a Period of Ten Years

I. S. ACRES. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [Trans. R. Soc. trop. Med. Hyg.] 44, 77-92, July, 1950. 11 refs.

In a country with widespread tsetse-fly population with no seasonal migration it is considered easier to control

the infectivity of comparatively few human beings by regular yearly visitation of villages and adequate treatment of all cases discovered, and thus to endeavour to empty the human reservoir of trypanosomes, rather than to attack the insect vector. Work carried out mainly by one doctor with a trained native staff in an area around the riverine town of Bolobo in the Belgian Congo resulted in a continuous decline in the incidence of sleeping sickness from 1.55 to 0.48% of the population during a period of 10 years. The disease was of moderate severity (class B) and 20% of the patients did not complain of any symptom. Among those who did complain headache was the common symptom, probably indicating nervous involvement and emphasizing the importance of going to the patient rather than waiting for him to come to hospital or dispensary. Diagnosis was by lymph-node puncture, repeated if necessary, and about one-quarter or one-third of the cases were subjected to lumbar puncture.

Treatment, which was carried out in hospital or in a rural dispensary, was with tryparsamide or its analogues in doses of 1 to 3 g. according either to age or body weight. The best results, with least visual impairment, were obtained with fairly large doses initially, followed by 10 smaller weekly doses. Children appeared to respond slightly better than adults, and the author attributes this to an intact reticulo-endothelial system. [Yet children have a higher malaria parasite rate than adults, and the tolerance of adults to malaria is associated with a scanty infection.] No increase in the incidence of resistant strains was noted, the cure rate averaging 85% and remaining approximately the same throughout the 10-year period.

Clement Chesterman

## MALARIA

#### 418. Single Intravenous Injections of Chloroquine in the Treatment of Falciparum Malaria: Toxic and Immediate Therapeutic Effects in 110 Cases

V. SCOTT. *American Journal of Tropical Medicine* [Amer. J. trop. Med.] 30, 503-510, July, 1950. 7 refs.

The author reports from Honduras on the efficacy of a single intravenous dose of chloroquine in the treatment of malaria. The dosage given ranged from 5.7 to 14.9 mg. per kg. body weight. Three techniques were employed—intravenous injection of the undiluted drug and of the drug diluted with saline, and slow infusion in saline. The first series consisted of 25 patients with malaria due to *Plasmodium falciparum*, of whom 22 were graded as acutely ill. One 10-ml. ampoule containing 400 mg. chloroquine base was diluted with 40 ml. saline and injected intravenously in not less than 6 minutes. There was a prompt clinical response, the temperature falling to normal in 2 to 22 hours and showing no significant rise thereafter. Parasites disappeared from the blood in 7 to 72 hours. It was found difficult to evaluate toxic symptoms in patients acutely ill, but the author notes dizziness as a common symptom associated with an average fall of 20 mm. Hg in the systolic blood pressure. In the next series, consisting of 10 patients, the contents of one 10-ml. ampoule containing 400 mg. of



chloroquine base was injected within 3 minutes. Therapeutic results were as good as before, but the toxic symptoms already noted were accentuated. In the third series the same amount of drug was diluted in 500 ml. of saline and infused intravenously over a period of 1 hour. Subjective reactions were absent and there was only an insignificant fall in blood pressure. No relapses have occurred in this series, but the period of observation has been short—less than 32 days. Because follow-up was impracticable all patients were given 1.5 g. of chloroquine to take orally on discharge. The infusion technique, which supplies fluid and electrolytes in addition to the antimalarial drug, is admirably suited to the treatment of the severely dehydrated case in hospital. In urgent cases in the field the drug can still be given intravenously by one of the other methods.

William Hughes

**419. The Course and Length of Malarial Infection at Different Ages.** (Возрастные особенности течения малярии и длительность малярийной инфекции в различных возрастных группах)

I. A. CHERVINSKIJ. Педиатрия [*Pediatrics*] No. 4, 3–8, July–Aug., 1950. 10 refs.

Since opinions are divided about the influence of age upon the course and duration of malarial infection, the author records his own observations, based on the material available at the clinical department of the Malaria Research Institute of Rostov-on-Don. This comprised cases of benign and malignant tertian malaria in children belonging to two groups: (a) up to the age of 4 years, and (b) from 4 to 15 years old.

In infants the acute phase of malaria frequently manifested a number of peculiarities. Thus, the infants had convulsions, there was dyspepsia, rigor and sweating were absent, the duration of the paroxysm was shorter than in adults, and the temperature curve was irregular. These gradually disappeared in older children; in those under the age of 4 they were less frequent and not so marked, while in those above this age convulsions were absent and the other symptoms were still milder. However, all these peculiarities are of secondary importance and do not affect the prognosis unfavourably. The duration of the infection in the different age groups showed no unusual features.

C. A. Hoare

**420. Clinical Features of Congenital Malaria.** (Клиника врожденной малярии)

I. A. BYSTRITSKIJ. Педиатрия [*Pediatrics*] No. 4, 9–11, July–Aug., 1950. 15 refs.

The author records observations on 28 cases of congenital malaria observed by him between 1934 and 1948 in Ufa, Kujbyshev, and Kursk. In 10 cases the weight at birth was below normal (1.5 to 2.7 kg.) while in 17 it was normal. It is assumed that in the former cases the infection was intrauterine through the placenta, while in the latter it took place during labour, as the result of the mixing of the maternal and foetal blood, owing to rupture of the vessels of the placenta or to puerperal trauma.

It is pointed out that congenital malaria is a grave condition which is liable to terminate fatally if it is not

diagnosed early and treated properly. If congenital malaria is treated systematically with mepacrine or quinine the prognosis may be quite favourable. The clinical features—splenitis, hepatitis, and anaemia—were confirmed by the finding of malaria parasites in blood films.

C. A. Hoare

**421. Congenital Malaria. Report of Three Cases**

B. S. JONES. *British Medical Journal* [*Brit. med. J.*] 2, 439–441, Aug. 19, 1950. 12 refs.

Most British and American writers consider that congenital malaria occurs only very rarely; English (*Brit. med. J.*, 1946, 1, 701) observed it once in 5,551 newborn children in Singapore. The present author records 3 cases of congenital subtertian malaria in non-Africans at the Creek Hospital, Lagos, Nigeria, all occurring between Feb. 11 and 25, 1949. The first child had English parents, the second French, and the third was a mulatto with a Scottish mother and an African father. All 3 children were healthy at birth and no malarial parasites were found in the mothers' blood on admission to hospital. Parturition was easy and normal in each case and the placenta was macroscopically healthy and intact.

Symptoms of malaria—fever, vomiting, and a slaty pallor—appeared 54 hours after birth in the first child, 77 hours after in the second, and 60 hours after in the third. Scanty subtertian rings were found in the blood of the umbilical cord at birth in 2 cases and in the blood of the other child when symptoms appeared. Quinine orally and intramuscularly had no apparent effect, nor had additional oral proguanil in the third case; the 3 children died 4, 4½, and 3½ days respectively after birth. Post-mortem examinations were not carried out.

In July and August, 1949, 23 children were born in the hospital and the cord blood was examined; malarial parasites were found in one only, but another child had a clinical attack of malaria 26 hours after birth. The author concludes that "among non-indigenous European women of relatively low immunity, infected with the Lagos strain of *Plasmodium falciparum*, congenital transmission of malaria is by no means rare". For treatment mepacrine 0.03 g. daily intramuscularly is advised and should be started on discovery of parasites in cord blood.

The author notes the contrast between hyperimmune indigenous populations among whom placental infection is very common but congenital malaria very rare, and non-indigenous individuals of low immunity, among whom placental infection is very rare but congenital malaria relatively less so; he regards the former condition as a result of immunity.

J. F. Corson

**422. Fulminating Tertian Malaria in Children.**

(Молниеносная трехдневная малярия у детей)  
G. I. GRENAUS, S. A. TROITSKIJ, and B. A. MILORADOVSKAJA. Педиатрия [*Pediatrics*] No. 4, 12–15, July–Aug., 1950.

Cases of a fulminating type of benign tertian malaria have been reported, chiefly from the central area of the Soviet Union. The pathogenesis of this serious con-

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dition is not yet clear, though a number of hypotheses have been advanced to explain it. In the present paper the authors describe the clinical course and epidemiology of fulminating malaria, which they have studied in children over a period of several years.

The great majority of cases (72.3%) occurred in the second quarter of the year, with a maximum in May, whereas there were only 8.4% in the first and 15.6% in the third quarter. The age incidence was as follows: up to 1 year 3.7%, 1 year to 6 years 13.4%, 7 to 12 years 40.7%, 13 to 17 years 23.5%, 18 to 29 years 12.3%, 30 years and older 6.4%. An analysis of the incidence of fulminating malaria in children showed that it was not correlated with the malarial incidence among them.

The disease runs an acute course, terminating fatally during the first, second, or third paroxysms of primary or relapse malaria. On the day preceding and during the morning of the fatal paroxysm the child may feel well. Then a rigor appears suddenly and is accompanied by severe headache, after which the paroxysm assumes a violent character: temperature rises, there are vomiting and convulsions, and the patient loses consciousness and dies within 1 to 3 hours, frequently before the physician can be summoned.

Necropsy reveals the presence of *Plasmodium vivax* in the blood, and typical pathological anatomical changes: cerebral oedema, flattening of the convolutions, and hyperplasia of the spleen.

The authors emphasize the importance of differential diagnosis of the fulminating type of benign tertian malaria from meningitis, tetanus, and uraemia, and of its immediate treatment, without waiting for the results of the examination of blood films.

C. A. Hoare

**423. Malaria in Infants and Young Children after Blood Transfusion.** (Малярия у детей грудного и раннего детского возраста после переливания крови)  
I. G. SITNITSKAJA. Педиатрия [*Pediatrics*] No. 4, 16-19 July-Aug., 1950.

In the U.S.S.R. blood transfusion is widely used in hospitals for children as a stimulating factor for increasing the resistance of the patient in a number of diseases. Under these conditions there have been cases of infection with malaria acquired from donors who had either concealed or were unaware of their own infection.

The author describes 25 cases of benign tertian malaria in infants and children up to the age of 3 years resulting from blood transfusion. The source of infection was traced to three ampoules, in two of which blood had been preserved for one day, while the third had been kept for 6 days. The last finding contradicts the generally accepted view that the malaria parasites in preserved blood die within 4 days.

The incubation period of transfusion malaria in children varied from 2 to 32 days. Its course and effects, which are described in some detail, follow the well-known pattern of induced malaria.

C. A. Hoare

**424. Action of Proguanil on *P. berghei*. Inhibition by p-Aminobenzoic Acid**

J. P. THURSTON. *Lancet* [*Lancet*] 2, 438, Sept. 30, 1950. 3 refs.

**425. Hepatic Fascioliasis.** (Фасциолез печени)  
D. A. LEVINA. Клиническая Медицина (*Klin. Med.*) *Mo sk.*] 28, No. 8, 57-61, Aug., 1950. 2 figs., 8 refs.

The author reports experience in 21 cases of hepatic fascioliasis. *Fasciola hepatica* infection of human subjects takes place orally through ingestion of infected water or fruit; the fluke reaches the liver by the duodenum and gall-bladder. In most of the cases general malaise, nausea, and fever were present. The chief complaint in all cases was of a constant pain under the right costal margin. The liver was usually enlarged and painful; 16 patients had had repeated severe attacks of right subcostal pain. There was a more or less intense eosinophilia, the count depending on the severity of the infection. It was highest at the beginning and gradually stabilized itself at about 7 to 10%. With it appeared a leucocytosis of 18,000 to 20,000 per c. mm. The diagnosis of this disease is made by finding the fasciola larvae in the stool or duodenal secretion. Repeated tests were necessary. In treatment 1.5 ml. of a 2% emetine solution twice daily was found effective in all cases. During treatment a steep rise in eosinophil count in the blood was noted and was thought to be due to a destruction of the fasciolae.

The author suggests that all cases of so-called "idiopathic eosinophilia" should be considered as cases of hepatic fascioliasis and treated with emetine.

N. Chatelain

**426. Genito-urinary Lesions in Schistosomiasis Mansoni.** (Lesões geniturinárias na esquistossomose mansoni)  
A. DE FREITAS ARMBRUST. *O Hospital* [*Hospital, Rio de J.*] 38, 177-210, Aug., 1950. 9 figs., bibliography.

Schistosomiasis mansoni in Brazil usually affects the portal system and the liver, and is accompanied by splenomegaly. There is no doubt, however, that it frequently infects the genito-urinary tract as well. The kidney is very rarely attacked, but the lower third of the ureter is frequently involved to such a degree that the lumen may become completely blocked. The bladder is the organ most frequently attacked, especially around the trigone; the membranous urethra also suffers. Other organs involved are the prostate, seminal vesicles, spermatic cord and epididymis, testis, and penis; the female genital tract may sometimes also be affected.

Most of this article is devoted to a survey of the literature dealing with the various aspects of schistosomiasis in all these organs. The author then describes 4 cases. In the first, encysted eggs were found in the cortex of the kidneys. The second patient complained of scrotal swellings of 20 years' duration; biopsy examination of the testicle showed cysts which were surrounded by lymphocytes, plasma cells, and eosinophils; the eggs were easily recognized as having lateral spines, and some were calcified. The third patient was a woman who underwent hysterectomy, eggs being found in the Fallopian tubes; these were surrounded by epithelioid cells, and there was giant-cell formation as well. The fourth case was one of infected seminal vesicles. The

author thinks that the kidneys suffer little when infected with *S. mansoni*; the infection is almost certainly blood-borne, for one egg was found in the afferent artery to a glomerulus (compare the origin of pulmonary bilharzial infection with *S. haematobium*). In severe cases a septicaemia must exist.

Paul B. Woolley

#### 427. The Treatment of Urinary Bilharzia in Egypt by Miracil D

J. NEWSOME and A. HALAWANI. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [Trans. R. Soc. trop. Med. Hyg.] 44, 67-76, July, 1950. 1 fig., 4 refs.

Therapeutic trials of "miracil A and D" in the treatment of urinary bilharziasis were carried out with special precautions to ensure that the patients were not harbouring immature worms from a recent invasion of cercariae, and that they did not become reinfected during treatment; these objects were achieved by treating prisoners who had been in jail for at least 6 months, or infected workmen from the Nile Valley who were employed in desert oil-fields near the Red Sea. The drug was given as uncoated compressed tablets placed in cachets to avoid the irritant effect on the mucous membranes. The dose was 1 g. morning and evening for 3 days only, followed by two similar courses at monthly intervals. This arrangement reduced the duration of the nausea and anorexia caused by the drug to a minimum, and the patients had largely forgotten about them before the next course was due. A special technique is described for detecting the excretion of small numbers of living eggs. The patient is first subjected to physical exertion and then passes urine. The centrifuged deposit is washed repeatedly in water and the final sediment is suspended in 2 ml. of fresh water for 1 hour in a flat cell; living miracidia are detected by projecting the greatly magnified image of the cell on to a screen by means of a simple projection-microscope.

The 17 prisoners treated were all very heavily infected, whereas the 17 oil-field workers treated were more lightly infected. The prisoners were all given three courses of treatment, but only those oil-workers whose urine was positive one month after the first course were treated again and no worker was given a third course. Thirteen prisoners were treated with miracil D; one month later 3 were cured (out of 9 examined), at 2 months 7 out of 13, at 3 months 9 out of 13, and at 6 months 10 out of 13. Four prisoners were treated with miracil A; after one month 3 were cured, and at 2 and 5 months all 4. Thirteen oil-workers were treated with miracil D; at the first month all 13 were apparently cured, but at 2 months one patient had relapsed and was given a second course. At 6 months 11 out of 13 were cured. Four workers were treated with miracil A, 2 being given a second course, but at 6 months only one patient was cured. During the courses of treatment abdominal colic, nausea, and light-headedness were common, but the patients did not refuse to cooperate. In this small series the therapeutic and toxic effects of miracil A were indistinguishable from those of miracil D.

Investigations were made into the possibility of reducing the unpleasant effects of miracil D. Giving the

uncoated tablets in cachets or gelatine capsules prevented the irritation of mouth and throat, but did not affect the gastro-intestinal symptoms. Enteric-coating diminished the gastro-intestinal effects, and in normal persons absorption of the drug was not diminished; but in patients infected with *Schistosoma mansoni* the intestine was more irritable and much of the drug was passed unabsorbed in the faeces, the concentration in the blood being correspondingly low. Miracil D is usually supplied as the hydrochloride and it is suggested that other salts, such as the mandelate or citrate, might be employed and would probably be less irritant.

F. Hawking

### OTHER INFECTIOUS DISEASES

#### 428. Effect of Terramycin in Yaws. (Ação da terramicina na boubá)

F. N. GUIMÃRES and J. TRAVASSOS. *O Hospital* [Hospital, Rio de J.] 38, 295-299, 1950. 9 refs.

Terramycin is a yellow crystalline substance obtained from *Streptomyces rimosus*, and used in the form of the hydrochloride. It can be given either by mouth or parenterally, and the only toxic symptoms seem to be diarrhoea and occasional nausea and vomiting. The dose is about 2 g. per day.

The present paper deals with its use in 4 cases of active and "infectious" yaws. The first 2 patients received the drug thrice daily by mouth, and the second 2 twice daily. It was considered wise to omit the nocturnal doses, in view of the possibility of using the drug on a large scale in the endemic rural areas. Within 24 hours there was less pain and inflammatory reaction, possibly due to the drug's action on intercurrent organisms. The active lesions were cured in from 6 to 16 days; as with other drugs, the cicatricial lesions took longer to disappear. Spirochaetes were found after 72 hours only in one case, but the reaction to the Wassermann test, as would be expected, remained positive 20 days after treatment.

The total doses used were 5 to 15 g. (ages 2 to 22 years) over a 10-day period. The therapeutic results were similar to those of penicillin, but the spirochaete did not disappear so rapidly as with the latter. The value of the drug is obvious, and its employment is being extended by the authors.

Paul B. Woolley

#### 429. Q Fever in California. I. Observations on Vaccination of Human Beings

G. MEIKLEJOHN and E. H. LENNETTE. *American Journal of Hygiene* [Amer. J. Hyg.] 52, 54-64, July, 1950. 1 fig., 35 refs.

As in other rickettsial infections, the investigation of Q fever entails considerable risk of infection for the laboratory staff engaged in it. The effect of immunization was therefore tested, formalized suspensions of *Rickettsia (Coxiella) burnetii* being used as vaccines after purification by ether extraction and separation of the aqueous phase. In 12 out of 23 persons complement-fixing antibodies developed to titres of 1 in 8 or more



4 weeks after a course of 3 weekly injections of 1 ml. of vaccine. A second course of three injections 8 weeks later produced a satisfactory response in 6 out of 8 persons who had not responded adequately to the first course. Although an accurate assessment of the rate of disappearance of antibodies was not possible, an 8-fold fall in titre in 22 weeks was sometimes noted, the fall beginning after 6 to 10 weeks. Thus, in order to maintain a titre of at least 1 in 64 in as many people as possible, blood was taken every 3 months and booster doses were given to those with inadequate titres. A number of general and local reactions, sterile abscess formation at the site of inoculation being the most troublesome, were noted with one batch of vaccine, but only after booster doses.

Rises in titre, occurring independently of booster doses, suggested that 6 immunized persons had developed subclinical infections. No manifest infection occurred among the immunized, but in one non-immunized person Q fever developed. The patient had been employed for 3 weeks in carrying out complement-fixation tests with inactivated antigens. Infection had apparently occurred from infected blood samples. There was a good response to aureomycin therapy (16 g. in 4 days). *R. burnetii* was isolated from the blood before, and for the first 2 days after, treatment was instituted.

D. G. ff. Edward

430. **Further Studies on the Morphology and Diagnosis of Q Fever.** (Weitere Befunde zur Morphologie und Diagnostik des Q-Fieber-Erregers) K. HERZBERG, H. HERZBERG-KREMMER, and H. URBACH. *Zentralblatt für Bakteriologie, Parasitenkunde und Infektionskrankheiten. I Abt., Originale [Zbl. Bakt. (I Abt., Orig.)]* 156, 14-23, Aug. 15, 1950. 13 figs., 19 refs.

By injecting *Rickettsia burnetii* into guinea-pigs' testes the authors were able to study the morphology of the development cycle of the causative agent of Q fever. The material containing *R. burnetii* was either citrated blood taken from infected guinea-pigs during the period of rise in body temperature, or spleen, liver, or lung tissue of infected mice, suitably ground up. This material was diluted 1 in 10 with physiological saline and injected in quantities of 0.25 ml. into the testes of guinea-pigs of 400 to 500 g. weight. The animals were killed, usually between the sixth and eighth day after the onset of the fever, and the testes removed under sterile conditions. Each testis was then cut in half in a sterile Petri dish, the surplus fluid from the cut surface was removed with sterile cotton wool, and impression preparations were made on sterile slides. The slides were left to dry for 3 days, stained in Giemsa solution (1 drop to 1 ml. water) for 6 hours without differentiation in alcohol, washed in tap water, and dried in an incubator. The testes were then used for further passages by grinding up in 1 in 100 dilution, or kept for histological examination after placing in 10% formalin.

The development cycle of *R. burnetii*, as deduced from such preparations, is as follows. Single rickettsiae invade the protoplasm of the histiocytes which soon appear in the infected organ, forming groups around

which vacuoles develop and in which rapid multiplication takes place. The vacuoles expand and thus enlarge the cell, flattening the nucleus and pushing it to the periphery. Finally the contents of the vacuoles empty into the interstitial space and the cycle starts afresh. Slide preparations made during the later stages suggest that the cells may regenerate. The numerous single and diplo-forms of the rickettsiae suggest multiplication by binary fission. Filamentous forms and chains may also be seen. The authors regard the vacuolated histiocytes as characteristic and diagnostic of Q fever. Rickettsiae could also be demonstrated in histological sections from infected testes and the morphological changes corresponded to those observed in impression preparations.

Citrated blood from clinically suspect human cases of Q fever was diluted 1 in 2 with saline and 1 ml. was injected intraperitoneally into a number of guinea-pigs. Citrated heart blood, diluted 1 in 10, from those animals which showed an increase of temperature between the 6th and 13th days was injected intraperitoneally into the testes and lungs of a number of fresh and immune guinea-pigs. Rise in temperature and demonstration of rickettsiae in the tissues of non-immune animals, and absence of reaction in the immune guinea-pigs allowed a diagnosis of Q fever to be made within 2 to 3 weeks.

K. S. Zinnemann

431. **Observations on Blastomycosis in Amazonia.** (Contribuição ao estudo das blastomicoses na Amazônia) F. N. GUIMÃRES and D. G. MACEDO. *O Hospital [Hospital, Rio de J.]* 38, 223-253, Aug., 1950. 15 figs., bibliography.

This is a long article dealing with two South American forms of blastomycosis; the first, known as keloid blastomycosis (with formation), is caused by *Glenosporella lobo*, and the second, South American blastomycosis, is caused by *Blastomyces brasiliensis*.

The keloid form is rare—9 cases in 20 years—and is found in the Amazon basin. It takes the form of a benign skin lesion, which may be present for 30 years; there is no general invasion, but the lymphatics may be involved. It is characterized by the formation of tumours and nodules resembling keloid tissue, and there is no surrounding inflammation; the nodules finally ulcerate. Epithelioid cells proliferate and tubercles are formed. Culture of the fungus is very difficult and it is almost non-pathogenic to laboratory animals. The disease is resistant to all antimycotic agents, and lesions frequently break down after operation.

The authors describe a case of the second type. This is a virulent infection which is always fatal. The lungs are specially involved and frequently the liver, spleen, and intestines. There is abscess formation and necrosis of tissue. In the case described the disease had started with vegetating ulcers in the mouth and nose, and necropsy showed that the disease had become disseminated. The lesions contained many parasites actively multiplying; these were easily cultured and proved pathogenic to laboratory animals.

Paul B. Woolley

See also Section Microbiology, Abstract 171.

# History of Medicine

## 432. The Historical Relationship between the Concept of Tumor and the Ending -oma

H. KEIL. *Bulletin of the History of Medicine [Bull. Hist. Med.]* 24, 352-377, July-Aug., 1950. Bibliography.

Although it is rather a neglected portion of the medical historian's field, the history of words and of medical nomenclature is as fruitful a study as is the history of men and ideas.

The ending "-oma" designates a tumour or swelling, irrespective of its nature: the Galenic conception of "tumour against Nature". By the Hippocratic writers the term carcinoma was by no means restricted to malignant growths, although to the mind of Celsus it did indicate cancer. The Hippocratic writers and Celsus employed the ending "-cele" to signify a hernial swelling such as bubonocoele, enterocoele, and so on. Galen's expression *oncos* or *oncoma* was the equivalent of *oedema* of the Hippocratic writers, in the sense of a swelling of the various "humours". The Arabian physicians exerted but little influence upon medical nomenclature, and it was during medieval times that the term *apostema* was used to describe a swelling or tumour. Severinus, in the seventeenth century, used the word *abscessus* in a similar sense, but soon this term became restricted to purulent collections. It was not until the eighteenth century that carcinoma came to be employed as a synonym for cancer, and not until the nineteenth century that the other "-omata", with which we are now so familiar, the lipoma, hygroma, epithelioma, and the like, became words in general use in medical circles. But even to-day the word tumour retains a sinister significance in the mind of the patient, and it is still necessary to be cautious in employing it. Nomenclature is not yet fixed, and the study of words appears to be desirable. [This useful and original paper is a scholarly production, and is accompanied by a bibliography of 110 references.]

Douglas Guthrie

## 433. Observations on Fused Kidneys with Horseshoe Configuration: the Contribution of Leonardo Botallo (1564)

J. A. BENJAMIN and D. M. SCHULLIAN. *Journal of the History of Medicine and Allied Sciences [J. Hist. Med.]* 5, 315-326, Summer, 1950. 14 figs., 30 refs.

Botallo was probably the first to describe and illustrate the fused kidney with horseshoe configuration when he wrote: *Concerning a monstrous kidney which was recently found*. His illustration is remarkably accurate, and shows the anomalous blood vessels which play so important a part in the development of the condition. It is noteworthy that he anticipated by four centuries the work of modern investigators. Botallo compared the horseshoe kidney with the normal kidney, but he stated that he had found four kidneys and only two ureters. His accurate description of the various vascular patterns is really remarkable, as it shows how the study of medical

history may assist present-day research. Botallo's account of the condition, which is reproduced in full in this paper, was followed, a century later, by similar observations by the Danish anatomist, Thomas Bartholin, and there have been many contributions to the problem since then. The recent work of Wilson of Rochester has elucidated the aetiology of horseshoe kidney, which has been produced experimentally in the rat foetus.

Douglas Guthrie

## 434. The Psychiatry of Paracelsus

I. GALDSTON. *Bulletin of the History of Medicine [Bull. Hist. Med.]* 24, 205-218, May-June, 1950. 35 refs.

It is timely to scrutinize the psychiatry of Paracelsus in this atomic age when the scientist has been compelled to take account of the meaning of life rather than leave the realm of the "why" to philosophers and content himself with the more explicable "how". The views of Paracelsus are of great interest to us to-day, because it was he who, long before the days of Freud, attempted to explain the mysterious interrelations of mind and body and broke away so violently from the mediaeval conceptions. For him anatomy was a dead subject. "It is the living body that teaches the physician health and disease, not the dead one". Moreover, he showed that man was but a part of his social environment, a mirror of his surroundings. Paracelsus went on to distinguish between the various forms of mental disorder. The feeble-minded, he said, were born simple, but the psychopathic are not born psychopathic. Indeed, Paracelsus was an exponent of psychosomatic medicine long before that ugly word was coined. He was not handicapped by that separation of body and soul which has caused so much confusion since the time of Descartes. To many minds to-day much of his teaching is simply crass superstition, yet he was not a mystic and, although he never envisaged psychiatry as a special subject, it is justifiable to speak of the psychiatry of Paracelsus. His effort to understand man in his physiological and psychological functions, within the framework of the universe and as a component of it, commands respect and attention. He believed in exhortation, persuasion, fasting, and prayer, and he set great store upon sleep. It is useless to attempt to modernize Paracelsus. He must be viewed in his contemporary setting, when it will be found that much of his thought has meaning and inspiration for the world to-day.

Douglas Guthrie

## 435. Humphry Davy's Contribution to Anaesthesia

F. F. CARTWRIGHT. *Proceedings of the Royal Society of Medicine [Proc. R. Soc. Med.]* 43, 571-578, July, 1950.

## 436. The History of the Vienna School of Medicine. (Zur Geschichte der Wiener Medizinischen Schule)

N. JAGIČ. *Wiener Klinische Wochenschrift [Wien. klin. Wschr.]* 62, 494-496, July 14, 1950.